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(54) Title: SYNTHETIC PEPTIDE INHIBITORS OF HIV TRANSMISSION

(57) Abstract

The present invention relates to peptides which exhibit potent anti-retroviral activity. The peptides of the invention comprise DP-178 (SEQ ID:1) peptide corresponding to amino acids 638 to 673 of the HIV-1_{LAI} gp41 protein, and fragments, analogs and homologs of DP-178. The invention further relates to the uses of such peptides as inhibitory of human and non-human retroviral, especially HIV, transmission to uninfected cells.

SYNTHETIC PEPTIDE INHIBITORS OF HIV TRANSMISSION1. INTRODUCTION

The present invention relates to DP-178 (SEQ ID:1), a peptide corresponding to amino acids 638 to 673 of the HIV-1_{LAI} transmembrane protein (TM) gp41, and portions, analogs, and homologs of DP-178 (SEQ ID:1), all of which exhibit anti-viral activity. Such anti-viral activity includes, but is not limited to, the inhibition of HIV transmission to uninfected CD-4⁺ cells. Further, the invention relates to the use of DP-178 (SEQ ID:1) and DP-178 fragments and/or analogs or homologs as inhibitors of human and non-human retroviral, especially HIV, transmission to uninfected cells. Still further, the invention relates to the use of DP-178 as a HIV subtype-specific diagnostic. The present invention also relates to antiviral peptides analogous to DP-107, a peptide corresponding to amino acids 558 to 595 of the HIV-1_{LAI} transmembrane protein (TM) gp41, that are present in other enveloped viruses. The present invention further relates to methods for identifying antiviral compounds that disrupt the interaction between DP-178 and DP-107, and/or between DP-107-like and DP-178-like peptides. The invention is demonstrated by way of a working example wherein DP-178 (SEQ ID:1), and a peptide whose sequence is homologous to DP-178 are each shown to be potent, non-cytotoxic inhibitors of HIV-1 transfer to uninfected CD-4⁺ cells. The invention is further demonstrated by working examples wherein peptides having antiviral and/or structural similarity to DP-107 and DP-178 are identified.

2. BACKGROUND OF THE INVENTION2.1. THE HUMAN IMMUNODEFICIENCY VIRUS

The human immunodeficiency virus (HIV) has been implicated as the primary cause of the slowly degenerative immune system disease termed acquired 5 immune deficiency syndrome (AIDS) (Barre-Sinoussi, F. et al., 1983, Science 220:868-870; Gallo, R. et al., 1984, Science 224:500-503). There are at least two distinct types of HIV: HIV-1 (Barre-Sinoussi, F. et al., 1983, Science 220:868-870; Gallo R. et al., 1984, 10 Science 224:500-503) and HIV-2 (Clavel, F. et al., 1986, Science 233:343-346; Guyader, M. et al., 1987, Nature 326:662-669). Further, a large amount of 15 genetic heterogeneity exists within populations of each of these types. Infection of human CD-4⁺ T-lymphocytes with an HIV virus leads to depletion of the cell type and eventually to opportunistic infections, neurological dysfunctions, neoplastic growth, and ultimately death.

HIV is a member of the lentivirus family of 20 retroviruses (Teich, N. et al., 1984, RNA Tumor Viruses, Weiss, R. et al., eds., CSH-Press, pp. 949-956). Retroviruses are small enveloped viruses that contain a diploid, single-stranded RNA genome, and 25 replicate via a DNA intermediate produced by a virally-encoded reverse transcriptase, an RNA-dependent DNA polymerase (Varus, H., 1988, Science 240:1427-1439). Other retroviruses include, for example, oncogenic viruses such as human T-cell 30 leukemia viruses (HTLV-I,-II,-III), and feline leukemia virus.

The HIV viral particle consists of a viral core, composed of capsid proteins, that contains the viral RNA genome and those enzymes required for early replicative events. Myristylated Gag protein forms an 35

outer viral shell around the viral core, which is, in turn, surrounded by a lipid membrane envelope derived from the infected cell membrane. The HIV envelope surface glycoproteins are synthesized as a single 160 Kd precursor protein which is cleaved by a cellular 5 protease during viral budding into two glycoproteins, gp41 and gp120. gp41 is a transmembrane protein and gp120 is an extracellular protein which remains non-covalently associated with gp41, possibly in a trimeric or multimeric form (HammarSKjold, M. and 10 Rekosh, D., 1989, *Biochem. Biophys. Acta* 989:269-280). HIV is targeted to CD-4⁺ cells because the CD-4 cell surface protein acts as the cellular receptor for the HIV-1 virus (Dalgleish, A. et al., 1984, *Nature* 312:763-767; Klatzmann et al., 1984, *Nature* 312:767- 15 768; Maddon et al., 1986, *Cell* 47:333-348). Viral entry into cells is dependent upon gp120 binding the cellular CD-4⁺ receptor molecules (McDougal, J.S. et al., 1986, *Science* 231:382-385; Maddon, P.J. et al., 1986, *Cell* 47:333-348) and thus explains HIV's tropism 20 for CD-4⁺ cells, while gp41 anchors the envelope glycoprotein complex in the viral membrane.

2.2. HIV TREATMENT

HIV infection is pandemic and HIV associated 25 diseases represent a major world health problem. Although considerable effort is being put into the successful design of effective therapeutics, currently no curative anti-retroviral drugs against AIDS exist. In attempts to develop such drugs, several stages of 30 the HIV life cycle have been considered as targets for therapeutic intervention (Mitsuya, H. et al., 1991, *FASEB J.* 5:2369-2381). For example, virally encoded reverse transcriptase has been one focus of drug development. A number of reverse-transcriptase- 35

targeted drugs, including 2',3'-dideoxynucleoside analogs such as AZT, ddI, ddC, and d4T have been developed which have been shown to be active against HIV (Mitsuya, H. *et al.*, 1991, *Science* 249:1533-1544). While beneficial, these nucleoside analogs are not 5 curative, probably due to the rapid appearance of drug resistant HIV mutants (Lander, B. *et al.*, 1989, *Science* 243:1731-1734). In addition, the drugs often exhibit toxic side effects such as bone marrow suppression, vomiting, and liver function 10 abnormalities.

Attempts are also being made to develop drugs which can inhibit viral entry into the cell, the earliest stage of HIV infection. Here, the focus has thus far been on CD4, the cell surface receptor for 15 HIV. Recombinant soluble CD4, for example, has been shown to inhibit infection of CD-4⁺ T-cells by some HIV-1 strains (Smith, D.H. *et al.*, 1987, *Science* 238:1704-1707). Certain primary HIV-1 isolates, however, are relatively less sensitive to inhibition 20 by recombinant CD-4 (Daar, E. *et al.*, 1990, *Proc. Natl. Acad. Sci. USA* 87:6574-6579). In addition, recombinant soluble CD-4 clinical trials have produced inconclusive results (Schooley, R. *et al.*, 1990, *Ann. Int. Med.* 112:247-253; Kahn, J.O. *et al.*, 1990, *Ann. Int. Med.* 112:254-261; Yarchoan, R. *et al.*, 1989, 25 *Proc. Vth Int. Conf. on AIDS*, p. 564, MCP 137).

The late stages of HIV replication, which involve crucial virus-specific secondary processing of certain viral proteins, have also been suggested as possible 30 anti-HIV drug targets. Late stage processing is dependent on the activity of a viral protease, and drugs are being developed which inhibit this protease (Erickson, J., 1990, *Science* 249:527-533). The

clinical outcome of these candidate drugs is still in question.

Attention is also being given to the development of vaccines for the treatment of HIV infection. The HIV-1 envelope proteins (gp160, gp120, gp41) have been shown to be the major antigens for anti-HIV antibodies present in AIDS patients (Barin, et al., 1985, *Science* 228:1094-1096). Thus far, therefore, these proteins seem to be the most promising candidates to act as antigens for anti-HIV vaccine development. To this end, several groups have begun to use various portions of gp160, gp120, and/or gp41 as immunogenic targets for the host immune system. See for example, Ivanoff, L. et al., U.S. Pat. No. 5,141,867; Saith, G. et al., WO 92/22,654; Shafferman, A., WO 91/09,872; Formoso, C. et al., WO 90/07,119. Clinical results concerning these candidate vaccines, however, still remain far in the future.

Thus, although a great deal of effort is being directed to the design and testing of anti-retroviral drugs, a truly effective, non-toxic treatment is still needed.

3. SUMMARY OF THE INVENTION

The present invention relates to DP-178 (SEQ 25 ID:1), a 36-amino acid synthetic peptide corresponding to amino acids 638 to 673 of the transmembrane protein (TM) gp41 from the HIV-1 isolate LAI, which exhibits potent anti-HIV-1 activity. As evidenced by the example presented below, in Section 6, the DP-178 (SEQ 30 ID:1) anti-viral activity is so high that, on a weight basis, no other known anti-HIV agent is effective at concentrations as low as those at which DP-178 (SEQ ID:1) exhibits its inhibitory effects. The invention further relates to those portions, analogs, and

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homologs of DP-178 which also show such antiviral activity. The antiviral activity of such DP-178 portions, analogs, and homologs, includes, but is not limited to the inhibition of HIV transmission to uninfected CD-4⁺ cells. The invention relates to the 5 use of DP-178 (SEQ ID:1) and DP-178 fragments and/or analogs or homologs. Such uses may include, but are not limited to, the use of the peptides as inhibitors of human and non-human retroviral, especially HIV, transmission to uninfected cells, and as type and/or 10 subtype-specific diagnostic tools.

An embodiment of the invention is demonstrated below wherein an extremely low concentration of DP-178 (SEQ ID:1), and very low concentrations of a DP-178 homolog (SEQ ID:3) are shown to be potent inhibitors 15 of HIV-1 mediated CD-4⁺ cell-cell fusion (*i.e.*, syncytial formation) and infection of CD-4⁺ cells by cell-free virus. Further, it is shown that DP-178 (SEQ ID:1) is not toxic to cells, even at concentrations 3 logs higher than the inhibitory 20 DP-178 (SEQ ID:1) concentration.

The invention also relates to analogous DP178 peptides in other enveloped viruses that demonstrate similar antiviral properties.

The invention further relates to peptides 25 analogous to DP-107, a peptide corresponding to amino acids 558-595 of the HIV-1_{LAI} transmembrane protein (TM) of gp41, that are present in other enveloped viruses, and demonstrate antiviral properties. The present invention is based, in part, on the surprising 30 discovery that the DP-107 and DP-108 domains of the gp41 protein non-covalently complex with each other, and that their interaction is necessary for the normal activity of the virus. The invention, therefore, further relates to methods for identifying antiviral 35

compounds that disrupt the interaction between DP-107 and DP-178, and/or between DP-107-like and DP-178-like peptides.

Embodiments of the invention are demonstrated, below, wherein peptides having structural and/or 5 similarity to DP-107 and DP-178 are identified.

3.1. DEFINITIONS

Peptides are defined herein as organic compounds comprising two or more amino acids covalently joined 10 by peptide bonds. Peptides may be referred to with respect to the number of constituent amino acids, i.e., a dipeptide contains two amino acid residues, a tripeptide contains three, etc. Peptides containing ten or fewer amino acids may be referred to as 15 oligopeptides, while those with more than ten amino acid residues are polypeptides.

Peptide sequences defined herein are represented by one-letter symbols for amino acid residues as follows:

- 20 A (alanine)
- R (arginine)
- N (asparagine)
- D (aspartic acid)
- C (cysteine)
- 25 Q (glutamine)
- E (glutamic acid)
- G (glycine)
- H (histidine)
- I (isoleucine)
- 30 L (leucine)
- K (lysine)
- M (methionine)
- F (phenylalanine)
- P (proline)

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S (serine)
T (threonine)
W (tryptophan)
Y (tyrosine)
V (valine)

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4. BRIEF DESCRIPTION OF THE FIGURES

FIG. 1. Amino acid sequence of DP-178 (SEQ ID:1) derived from HIV_{LAI}; DP-178 homologs derived from HIV-1_{SP2} (DP-185; SEQ ID:3), HIV-1_{RF} (SEQ ID:4), and HIV-1_{MN} (SEQ ID:5); DP-178 homologs derived from amino acid sequences of two prototypic HIV-2 isolates, namely, HIV-2_{rod} (SEQ ID:6) and HIV-2_{NHZ} (SEQ ID:7); control peptides: DP-180 (SEQ ID:2), a peptide incorporating the amino acid residues of DP-178 in a scrambled sequence; DP-118 (SEQ ID:10) unrelated to DP-178, which inhibits HIV-1 cell free virus infection; DP-125 (SEQ ID:8), unrelated to DP-178, was also previously shown to inhibit HIV-1 cell free virus infection (Wild *et al.*, 1992, Proc. Natl. Acad. Sci USA 89:10,537-10,541); DP-116 (SEQ ID:9), unrelated to DP-178 had previously been shown to be negative for inhibition of HIV-1 infection using the cell-free virus infection assay (Wild, *et al.*, 1992, Proc. Natl. Acad. Sci USA 89:10,537-10,541). Throughout the figures, the one letter amino acid code is used.

FIG. 2. Inhibition of HIV-1 cell-free virus infection by synthetic peptides. IC50 refers to the concentration of peptide that inhibits RT production from infected cells by 50% compared to the untreated control. Control: the level of RT produced by untreated cell cultures infected with the same level of virus as treated cultures.

FIG. 3. Inhibition of HIV-1 and HIV-2 cell-free virus infection by the synthetic peptide DP-178 (SEQ 35

ID:1). IC50: concentration of peptide that inhibits RT production by 50% compared to the untreated control. Control: Level of RT produced by untreated cell cultures infected with the same level of virus as treated cultures.

5 FIG. 4A. Fusion Inhibition Assay. DP-178 (SEQ ID:1) inhibition of HIV-1 prototypic isolate-mediated syncytia formation. Data represents the number of virus-induced syncytia per cell.

10 FIG. 4B. Fusion Inhibition Assay. DP-180 (SEQ ID:2): scrambled control peptide. DP-185 (SEQ ID:3): DP-178 homolog derived from HIV-1_{SF2} isolate. Control: number of syncytia produced in the absence of peptide.

15 FIG. 5. Fusion inhibition assay: HIV-1 vs. HIV-2. Data represents the number of virus-induced syncytia per well. ND: not done.

FIG. 6. Cytotoxicity study of DP-178 (SEQ ID:1) and DP-116 (SEQ ID:9) on CEM cells. Cell proliferation data is shown.

20 FIG. 7. Schematic representation of HIV-gp41 and maltose binding protein (MBP)-gp41 fusion proteins. DP107 and DP178 are synthetic peptides based on the two putative helices of gp41. The letter P in the DP107 boxes denotes an Ile to Pro mutation at amino acid number 578. Amino acid residues are
25 numbered according to Meyers et al., Human Retroviruses and AIDS, 1991, Theoret. Biol. and Biophys. Group, Los Alamos Natl. Lab., Los Alamos, NM.

FIG. 8. A point mutation alters the conformation and anti-HIV activity of M41.

30 FIG. 9. Abrogation of DP178 anti-HIV activity. Cell fusion assays were carried out in the presence of 10 nM DP178 and various concentrations of M41Δ178 or M41PΔ178.

FIG. 10. Binding of DP178 to leucine zipper of gp41 analyzed by ELISA.

FIG. 11A-B. Models for a structural transition in the HIV-1 TM protein. Two models are proposed which indicate a structural transition from a native 5 oligomer to a fusogenic state following a trigger event (possibly gp120 binding to CD4). Common features of both models include (1) the native state is held together by noncovalent protein-protein interactions to form the heterodimer of gp120/41 and 10 other interactions, principally through gp41 interactive sites, to form homo-oligomers on the virus surface of the gp120/41 complexes; (2) shielding of the hydrophobic fusogenic peptide at the N-terminus (F) in the native state; and (3) the leucine zipper 15 domain (DP107) exists as a homo-oligomer coiled coil only in the fusogenic state. The major differences in the two models include the structural state (native or fusogenic) in which the DP107 and DP178 domains are complexed to each other. In the first model (A; FIG. 20 20) this interaction occurs in the native state and in B during the fusogenic state. When triggered, the fusion complex in the model depicted in (A) is generated through formation of coiled-coil interactions in homologous DP107 domains resulting in 25 an extended α -helix. This conformational change positions the fusion peptide for interaction with the cell membrane. In the second model (B; FIG. 11B), the fusogenic complex is stabilized by the association of the DP178 domain with the DP107 coiled-coil.

30 FIG. 12. Motif design using heptad repeat positioning of amino acids of known coiled-coils.

FIG. 13. Motif design using proposed heptad repeat positioning of amino acids of DP-107 and DP-178.

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FIG. 14. Hybrid motif design crossing GCN4 and DP-107.

FIG. 15. Hybrid motif design crossing GCN4 and DP-178.

5 FIG. 16. Hybrid motif design 107x178x4, crossing DP-107 and DP-178. This motif was found to be the most consistent at identifying relevant DP-107-like and DP-178-like peptide regions.

10 FIG. 17. Hybrid motif design ALLMOTI5, crossing GCN4, DP-107, and DP-178.

15 FIG. 18. Hybrid motif design crossing GCN4, DP-107, DP-178, c-Fos c-Jun, c-Myc, and Flu Loop 36.

20 FIG. 19. Motifs designed to identify N-terminal proline-leucine zipper motifs.

25 FIG. 20. Search results for HIV-1 (BRU isolate) envelope protein gp41. Sequence search motif designations: Spades (♦): 107x178x4; Hearts (♥) ALLMOTI5; Clubs (♣): PLZIP; Diamonds (♦): transmembrane region (the putative transmembrane domains were identified using a PC/Gene program designed to search for such peptide regions). Asterisk (*): Lupas method. The amino acid sequences identified by each motif are bracketed by the respective characters. Representative sequences chosen based on all searches are underlined and in bold. DP-107 and DP-178 sequences are marked, and additionally double-underlined and italicized.

30 FIG. 21. Search results for human respiratory syncytial virus (RSV) strain A2 fusion glycoprotein F1. Sequence search motif designations are as in FIG. 20.

35 FIG. 22. Search results for simian immunodeficiency virus (SIV) envelope protein gp41 (AGM3 isolate). Sequence search motif designations are as in FIG. 20.

FIG. 23. Search results for canine distemper virus (strain Onderstepoort) fusion glycoprotein 1. Sequence search motif designations are as in FIG. 20.

5 FIG. 24. Search results for newcastle disease virus (strain Australia-Victoria/32) fusion glycoprotein F1. Sequence search motif designations are as in FIG. 20.

10 FIG. 25. Search results for human parainfluenza 3 virus (strain NIH 47885) fusion glycoprotein F1. Sequence search motif designations are as in FIG. 20.

15 FIG. 26. Search results for influenza A virus (strain A/AICHI/2/68) hemagglutinin precursor HA2. Sequence search designations are as in FIG. 20.

20 FIG. 27. Coiled-coil structural similarity and anti-RSV antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 48-amino acid RSV F2 peptide which spans sequences identified utilizing the computer-assisted searches described herein. For the exact location and motifs utilized, see FIG. 21. "+" symbols are relative indicators of either structural similarity or antiviral activity, with a greater number of "+" symbols indicating a higher relative similarity or antiviral activity.

25 FIG. 28. Coiled-coil structural similarity and anti-RSV antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 53-amino acid RSV F1 peptide which spans sequences identified utilizing the computer-assisted searches described herein. See FIG. 21 for the exact location and motifs used. "+" symbols are as described for FIG. 27.

30 FIG. 29. Coiled-coil structural similarity and anti-human parainfluenza 3 virus (HPF3) antiviral activity of 35-mer peptides synthesized utilizing the

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sequence of a 56-amino acid HPF3 peptide which spans sequences identified utilizing computer-assisted searches described herein. For the exact location and motifs utilized, see FIG. 25. "+" symbols are as described in FIG. 27.

5 FIG. 30. Coiled-coil structural similarity and anti-HPF3 antiviral activity of 35-mer peptides synthesized utilizing the sequence of a 70-amino acid HPF3 peptide which spans sequences identified utilizing the computer-assisted searches described
10 herein. For the exact location and motifs utilized, see FIG. 25. "+" symbols are as described in FIG. 27.

5. DETAILED DESCRIPTION OF THE INVENTION

Described herein are peptides that exhibit potent
15 antiviral activity. These peptides include DP-178 (SEQ ID:1), a gp41-derived 36 amino acid peptide, fragments and/or analogs of DP-178, and peptides which are homologous to DP-178. In addition, these peptides may include peptides exhibiting anti-viral activity
20 which are analogous to DP-107, a 38 amino acid peptide corresponding to residues 558 to 595 of the HIV-1_{LAI} transmembrane (TM) gp41 protein, and which are present in other enveloped viral proteins. Also described here are assays for testing the antiviral activities
25 of such peptides. The present invention is based, in part, of the surprising discovery that the DP-107 and DP-178 domains of the gp41 protein complex with each other via non-covalent protein-protein interactions which are necessary for normal activity of the virus.
30 As such, methods are described for the identification of antiviral compounds that disrupt the interaction between DP-107 and DP-178 peptides, and between DP-107-like and DP-178-like peptides. Finally, the use of the peptides of the invention as inhibitors of non-
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human and human viral and retroviral, especially HIV, transmission are detailed, as is the use of the peptides as diagnostic indicators of the presence of specific, viruses, especially retroviruses.

While not limited to any theory of operation, the 5 following model is proposed to explain the potent anti-HIV activity of DP178, based, in part, on the experiments described in the working examples, infra. In the viral protein, gp41, DP178 corresponds to a putative α -helix region located in the C-terminal end 10 of the gp41 ectodomain, and appears to associate with a distal site on gp41 whose interactive structure is influenced by the leucine zipper motif, a coiled-coil structure, referred to as DP107. The association of these two domains may reflect a molecular linkage or 15 "molecular clasp" intimately involved in the fusion process. It is of interest that mutations in the C-terminal α -helix motif of gp41 (i.e., the D178 domain) tend to enhance the fusion ability of gp41, whereas mutations in the leucine zipper region (i.e., 20 the DP107 domain) decrease or abolish the fusion ability of the viral protein. It may be that the leucine zipper motif is involved in membrane fusion while the C-terminal α -helix motif serves as a 25 molecular safety to regulate the availability of the leucine zipper during virus-induced membrane fusion.

On the basis of the foregoing, two models are proposed of gp41-mediated membrane fusion which are schematically shown in FIG. 11A-B. The reason for proposing two models is that the temporal nature of 30 the interaction between the regions defined by DP107 and DP178 cannot, as yet, be pinpointed. Each model envisions two conformations for gp41 - one in a "native" state as it might be found on a resting virion. The other in a "fusogenic" state to reflect 35

conformational changes triggered following binding of gp120 to CD4 and just prior to fusion with the target cell membrane. The strong binding affinity between gp120 and CD4 may actually represent the trigger for the fusion process obviating the need for a pH change

5 such as occurs for viruses that fuse within intracellular vesicles. The two major features of both models are: (1) the leucine zipper sequences (DP107) in each chain of oligomeric envelope are held apart in the native state and are only allowed access

10 to one another in the fusogenic state so as to form the extremely stable coiled-coils, and (2) association of the DP178 and DP107 sites as they exist in gp41 occur either in the native or fusogenic state. FIG. 11A depicts DP178/DP107 interaction in the native

15 state as a molecular class. On the other hand, if one assumes that the most stable form of the envelope occurs in the fusogenic state, the model in FIG. 11B can be considered.

When synthesized as peptides, both DP107 and

20 DP178 are potent inhibitors of HIV infection and fusion, probably by virtue of their ability to form complexes with viral gp41 and interfere with its fusogenic process; e.g., during the structural transition of the viral protein from the native

25 structure to the fusogenic state, the DP178 and DP107 peptides may gain access to their respective binding sites on the viral gp41, and exert a disruptive influence. DP107 peptides which demonstrate anti-HIV activity are described in Applicants' co-pending

30 application Serial No. 07/927,532, filed August 7, 1992, which is incorporated by reference herein in its entirety.

As shown in the working examples, infra, a truncated recombinant gp41 protein corresponding the

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ectodomain of gp41 containing both DP107 and DP178 domains (excluding the fusion peptide, transmembrane region and cytoplasmic domain of gp41) did not inhibit HIV-1 induced fusion. However, when a single mutation was introduced to disrupt the coiled-coil structure of 5 the DP107 domain -- a mutation which results in a total loss of biological activity of DP107 peptides -- the inactive recombinant protein was transformed to an active inhibitor of HIV-1 induced fusion. This transformation may result from liberation of the 10 potent DP178 domain from a molecular clasp with the leucine zipper, DP107 domain.

For clarity of discussion, the invention will be described for DP178 peptide inhibitors of HIV. However, the principles may be analogously applied to 15 other fusogenic enveloped viruses, including but not limited to those viruses containing the peptides listed in Tables V through X, below.

5.1. DP-178 AND DP-178-LIKE PEPTIDES

20 The peptide DP-178 (SEQ ID:1) of the invention corresponds to amino acid residues 638 to 673 of the transmembrane protein gp41 from the HIV-1_{LAI} isolate, and has the 36 amino acid sequence (reading from amino to carboxy terminus):

25

NH2-YTSLIHSLLIEESQNQQEKNEQELLELDKWASLWNWF-COOH (SEQ ID:1)

In addition to the full-length DP-178 (SEQ ID:1) 36-mer, the peptides of the invention may include 30 truncations of the DP-178 (SEQ ID:1) peptide which exhibit antiviral activity. Such truncated DP-178 (SEQ ID:1) peptides may comprise peptides of between 3 and 36 amino acid residues (*i.e.*, peptides ranging in size from a tripeptide to a 36-mer polypeptide), and 35

may include but are not limited to those listed in Tables I and II, below. Peptide sequences in these tables are listed from amino (left) to carboxy (right) terminus. "X" may represent an amino group (-NH₂) and "Z" may represent a carboxyl (-COOH) group.

5 Alternatively, as described below, "X" and/or "Z" may represent a hydrophobic group, an acetyl group, a Fmoc group, an amido group, or a covalently attached macromolecule.

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TABLE I
DP-178 (SEQ ID:1) CARBOXY TRUNCATIONS

X-YTS-Z
 X-YTSL-Z
 X-YTSLI-Z
 X-YTSLIH-Z
 5 X-YTSLIHS-Z
 X-YTSLIHSL-Z
 X-YTSLIHSLI-Z
 X-YTSLIHSLIE-Z
 X-YTSLIHSLIEE-Z
 X-YTSLIHSLIES-Z
 X-YTSLIHSLIESQ-Z
 10 X-YTSLIHSLIESQN-Z
 X-YTSLIHSLIESQNZ-Z
 X-YTSLIHSLIESQNQQ-Z
 X-YTSLIHSLIESQNQQE-Z
 X-YTSLIHSLIESQNQQEK-Z
 X-YTSLIHSLIESQNQQEKN-Z
 X-YTSLIHSLIESQNQQEKNE-Z
 X-YTSLIHSLIESQNQQEKNEQ-Z
 15 X-YTSLIHSLIESQNQQEKNEQE-Z
 X-YTSLIHSLIESQNQQEKNEQEL-Z
 X-YTSLIHSLIESQNQQEKNEQELL-Z
 X-YTSLIHSLIESQNQQEKNEQELLE-Z
 X-YTSLIHSLIESQNQQEKNEQELLED-Z
 X-YTSLIHSLIESQNQQEKNEQELLELDK-Z
 20 X-YTSLIHSLIESQNQQEKNEQELLELDKW-Z
 X-YTSLIHSLIESQNQQEKNEQELLELDKWA-Z
 X-YTSLIHSLIESQNQQEKNEQELLELDKWAS-Z
 X-YTSLIHSLIESQNQQEKNEQELLELDKWASL-Z
 X-YTSLIHSLIESQNQQEKNEQELLELDKWASLW-Z
 X-YTSLIHSLIESQNQQEKNEQELLELDKWASLWN-Z
 X-YTSLIHSLIESQNQQEKNEQELLELDKWASLWNW-Z
 X-YTSLIHSLIESQNQQEKNEQELLELDKWASLWNWF-Z

25 The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group,
 including but not limited to carbobenzoyl, dansyl, or
 30 T-butyloxycarbonyl; an acetyl group; a 9-
 fluorenylmethoxy-carbonyl (FMOC) group; a
 macromolecular carrier group including but not limited
 to lipid-fatty acid conjugates, polyethylene glycol,
 or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a
 T-butyloxycarbonyl group; a macromolecular carrier
 35 group including but not limited to lipid-fatty acid
 conjugates, polyethylene glycol, or carbohydrates.

TABLE II
DP-178 (SEQ ID:1) AMINO TRUNCATIONS

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X-NWF-Z
X-WNWF-Z
X-LWNWF-Z
X-SLWNWF-Z
X-ASLWNWF-Z
X-WASLWNWF-Z
X-KWASLWNWF-Z
X-DKWASLWNWF-Z
X-LDKWASLWNWF-Z
X-ELDKWASLWNWF-Z
X-LELDKWASLWNWF-Z
X-LLELDKWASLWNWF-Z
X-ELLELDKWASLWNWF-Z
X-QELLELDKWASLWNWF-Z
X-EQELLELDKWASLWNWF-Z
X-NEQELLELDKWASLWNWF-Z
X-KNEQELLELDKWASLWNWF-Z
X-EKNEQELLELDKWASLWNWF-Z
X-QEKNEQELLELDKWASLWNWF-Z
X-QQEKNEQELLELDKWASLWNWF-Z
X-NQQEKNEQELLELDKWASLWNWF-Z
X-QNQQEKNEQELLELDKWASLWNWF-Z
X-SQNQQEKNEQELLELDKWASLWNWF-Z
X-ESQNQQEKNEQELLELDKWASLWNWF-Z
X-EESQNQQEKNEQELLELDKWASLWNWF-Z
X-IEESQNQQEKNEQELLELDKWASLWNWF-Z
X-LIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-SLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-HSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-IHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-LIHSLLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-SLIHSLLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-TSLIHSLLIEESQNQQEKNEQELLELDKWASLWNWF-Z
X-YTSLIHSLLIEESQNQQEKNEQELLELDKWASLWNWF-Z

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The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoyl, dansyl, or 30 T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier 35 group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

The antiviral peptides of the invention also include analogs of DP-178 and/or DP-178 truncations which may include, but are not limited to, peptides comprising the DP-178 (SEQ ID:1) sequence, or DP-178 truncated sequence, containing one or more amino acid 5 substitutions, insertions and/or deletions. Analogs of DP-178 homologs, described below, are also within the scope of the invention. The DP-178 analogs of the invention exhibit antiviral activity, and may, further, possess additional advantageous features, 10 such as, for example, increased bioavailability, and/or stability, or reduced host immune recognition.

HIV-1 and HIV-2 envelope proteins are structurally distinct, but there exists a striking amino acid conservation within the DP-178- 15 corresponding regions of HIV-1 and HIV-2. The amino acid conservation is of a periodic nature, suggesting some conservation of structure and/or function. Therefore, one possible class of amino acid 20 substitutions would include those amino acid changes which are predicted to stabilize the structure of the DP-178 peptides of the invention.

Amino acid substitutions may be of a conserved or non-conserved nature. Conserved amino acid 25 substitutions consist of replacing one or more amino acids of the DP-178 (SEQ ID:1) peptide sequence with amino acids of similar charge, size, and/or hydrophobicity characteristics, such as, for example, a glutamic acid (E) to aspartic acid (D) amino acid 30 substitution. When only conserved substitutions are made, the resulting peptide is functionally equivalent to DP-178 (SEQ ID:1) or the DP-178 peptide from which it is derived. Non-conserved substitutions consist of 35 replacing one or more amino acids of the DP-178 (SEQ ID:1) peptide sequence with amino acids possessing dissimilar charge, size, and/or hydrophobicity

characteristics, such as, for example, a glutamic acid (E) to valine (V) substitution.

Amino acid insertions may consist of single amino acid residues or stretches of residues ranging from 2 to 15 amino acids in length. One or more insertions 5 may be introduced into DP-178 (SEQ ID:1), DP-178 fragments, analogs and/or DP-178 homologs (described below).

Deletions of DP-178 (SEQ ID:1), DP-178 fragments, 10 analogs, and/or DP-178 homologs (described below) are also within the scope of the invention. Such deletions consist of the removal of one or more amino acids from the DP-178 or DP-178-like peptide sequence, with the lower limit length of the resulting peptide 15 sequence being 4 to 6 amino acids. Such deletions may involve a single contiguous or greater than one discrete portion of the peptide sequences.

The peptides of the invention may further include homologs of DP-178 (SEQ ID:1) and/or DP-178 20 truncations which exhibit antiviral activity. Such DP-178 homologs are peptides whose amino acid sequences are comprised of the amino acid sequences of peptide regions of other (i.e., other than HIV-1_{LAI}) viruses that correspond to the gp41 peptide region 25 from which DP-178 (SEQ ID:1) was derived. Such viruses may include, but are not limited to, other HIV-1 isolates and HIV-2 isolates. DP-178 homologs derived from the corresponding gp41 peptide region of other (i.e., non HIV-1_{LAI}) HIV-1 isolates may include, 30 for example, peptide sequences as shown below.

30 NH₂-YTNTIYTLLEESQNQQEKNEQELLELDKWASLWNWF-COOH (DP-185; SEQ ID:3);

35 NH₂-YTGIIYNLLEESQNQQEKNEQELLELDKWANLWNWF-COOH (SEQ ID:4);

NH₂-YTSLIYSLLEKSQIQQQEKNEQELLELDKWASLWNWF-COOH (SEQ ID:5).

SEQ ID:3 (DP-185), SEQ ID:4, and SEQ ID:5 are derived from HIV-1_{SP2}, HIV-1_{RF}, and HIV-1_{MN} isolates, respectively. Underlined amino acid residues refer to 5 those residues that differ from the corresponding position in the DP-178 (SEQ ID:1) peptide. One such DP-178 homolog, DP-185 (SEQ ID:3), is described in the Working Example presented in Section 6, below, where 10 it is demonstrated that DP-185 (SEQ ID:3) exhibits antiviral activity. The DP-178 homologs of the invention may also include truncations, amino acid substitutions, insertions, and/or deletions, as 15 described above.

20 In addition, striking similarities, as shown in FIG. 1, exist within the regions of HIV-1 and HIV-2 isolates which correspond to the DP-178 sequence. A DP-178 homolog derived from the HIV-2_{NIHZ} isolate has the 36 amino acid sequence (reading from amino to carboxy terminus):

25 NH₂-LEANISQSLEQAQIQQQEKNMYELQKLNSWDVFTNWZ-COOH (SEQ ID:7)

30 Table III and Table IV show some possible truncations of the HIV-2_{NIHZ} DP-178 homolog, which may comprise peptides of between 3 and 36 amino acid residues (i.e., peptides ranging in size from a tripeptide to a 36-mer polypeptide). Peptide sequences in these tables are listed from amino (left) to carboxy (right) terminus. "X" may represent an amino group (-NH₂) and "Z" may represent a carboxyl (-COOH) group. Alternatively, as described below, "X" and/or "Z" may represent a hydrophobic group, an acetyl group, a FMOC group, an amido group, or a covalently attached macromolecule, as described below.

35

TABLE IIIHIV-2_{NH2} DP-178 homolog carboxy truncations.

X-LEA-Z
 X-LEAN-Z
 X-LEANI-Z
 X-LEANIS-Z
 5 X-LEANISQ-Z
 X-LEANISQS-Z
 X-LEANISQSL-Z
 X-LEANISQSLE-Z
 X-LEANISQSLEQ-Z
 X-LEANISQSLEQA-Z
 X-LEANISQSLEQAQ-Z
 10 X-LEANISQSLEQAQI-Z
 X-LEANISQSLEQAQIQ-Z
 X-LEANISQSLEQAQIQQ-Z
 X-LEANISQSLEQAQIQQE-Z
 X-LEANISQSLEQAQIQQEK-Z
 X-LEANISQSLEQAQIQQEKN-Z
 X-LEANISQSLEQAQIQQEKNM-Z
 X-LEANISQSLEQAQIQQEKNMY-Z
 15 X-LEANISQSLEQAQIQQEKNMYE-Z
 X-LEANISQSLEQAQIQQEKNMYEL-Z
 X-LEANISQSLEQAQIQQEKNMYELQ-Z
 X-LEANISQSLEQAQIQQEKNMYELQK-Z
 X-LEANISQSLEQAQIQQEKNMYELQKL-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-S-Z
 20 X-LEANISQSLEQAQIQQEKNMYELQKLN-SW-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWD-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDV-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVF-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVFT-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVFTN-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVFTNW-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLN-SWDVFTNWL-Z

25 The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group,
 including but not limited to carbobenzoyl, dansyl, or
 30 T-butyloxycarbonyl; an acetyl group; a 9-
 fluorenylmethoxy-carbonyl (FMOC) group; a
 macromolecular carrier group including but not limited
 to lipid-fatty acid conjugates, polyethylene glycol,
 or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a
 T-butyloxycarbonyl group; a macromolecular carrier
 35 group including but not limited to lipid-fatty acid
 conjugates, polyethylene glycol, or carbohydrates.

TABLE IV

HIV-2_{NIHZ} DP-178 homolog amino truncations.

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X-NWL-Z
 X-TNWL-Z
 X-FTNWL-Z
 X-VFTNWL-Z
 X-DVFTNWL-Z
 X-WDVFTNWL-Z
 X-SWDVFTNWL-Z
 X-NSWDVFTNWL-Z
 X-LNSWDVFTNWL-Z
 X-KLNSWDVFTNWL-Z
 X-QKLNSWDVFTNWL-Z
 X-LQKLNSWDVFTNWL-Z
 X-ELQKLNSWDVFTNWL-Z
 X-YELQKLNSWDVFTNWL-Z
 X-MYELQKLNSWDVFTNWL-Z
 X-NMYELQKLNSWDVFTNWL-Z
 X-KNMYELQKLNSWDVFTNWL-Z
 X-EKNMYELQKLNSWDVFTNWL-Z
 X-QEKNMYELQKLNSWDVFTNWL-Z
 X-QQEKNMYELQKLNSWDVFTNWL-Z
 X-IQQEKNMYELQKLNSWDVFTNWL-Z
 X-QIQQEKNMYELQKLNSWDVFTNWL-Z
 X-AQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-QAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-EQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-LEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-SLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-QSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-SQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-ISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-NISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-ANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-EANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z

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The one letter amino acid code is used.

Additionally,

"X" may represent an amino group, a hydrophobic group, including but not limited to carbobenzoyl, dansyl, or 30 T-butyloxycarbonyl; an acetyl group; a 9-fluorenylmethoxy-carbonyl (FMOC) group; a macromolecular carrier group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

"Z" may represent a carboxyl group; an amido group; a T-butyloxycarbonyl group; a macromolecular carrier 35 group including but not limited to lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates.

**5.2. DP-107 and DP-178 ANALOGOUS
ANTIVIRAL PEPTIDES**

Peptide sequences functionally corresponding, and thus analogous to, the DP-178 sequences of the invention, described, above, in Section 5.1 may be 5 found in other, non-HIV-1 envelope viruses. Further, peptide sequences functionally corresponding, and thus analogous to, DP-107, an HIV-1-derived antiviral peptide, may also be found in other, non-HIV-1 envelope viruses. DP-107 is a 38 amino acid peptide 10 corresponding to residues 558 to 595 of HIV-1_{LAI} transmembrane (TM) gp41 protein, which exhibits potent anti-viral activity. DP-107 is more fully described in Applicant's co-pending U.S. Patent Application Ser. No. 07/927,532. These DP-107-like and DP-178-like 15 analogous peptides and present in TM proteins of envelope viruses and preferably exhibit antiviral activity, most preferably antiviral activity which is specific to the virus in which their native sequences are found.

20 DP-107-like and DP-178-like peptides may be identified, for example, by utilizing a computer-assisted search strategy such as that described and demonstrated, below, in the Examples presented in Sections 9 through 16. The search strategy identifies 25 regions in other viruses that are similar in predicted secondary structure to DP-107 and DP-178.

This search strategy is described fully, below, in the Example presented in Section 9. While this search strategy is based, in part, on a primary amino 30 acid motif deduced from DP-107 and DP-178, it is not based solely on searching for primary amino acid sequence homologies, as such protein sequence homologies exist within, but not between major groups of viruses. For example, primary amino acid sequence 35 homology is high within the TM protein of different

strains of HIV-1 or within the TM protein of different isolates of simian immunodeficiency virus (SIV). Primary amino acid sequence homology between HIV-1 and SIV, however, is low enough so as not to be useful. It is not possible, therefore, to find DP-107 or DP-5 178-like peptides within other viruses, whether structurally, or otherwise, based on primary sequence homology, alone.

Further, while it would be potentially useful to identify primary sequence arrangements of amino acids 10 based on the physical chemical characteristics of different classes of amino acids rather than based on the specific amino acids themselves, for instance, a by concentrating on the coiled-coil nature of the peptide sequence, a computer algorithm designed by 15 Lupas et al. to identify such coiled-coil propensities of regions within proteins (Lupas, A., et al., 1991 *Science* 252:1162-1164) is inadequate for identifying protein regions analogous to DP-107 or DP-178.

Specifically, analysis of HIV-1 gp160 (containing 20 both gp120 and gp41) using the Lupas algorithm does not identify the coiled-coil region within DP-107. It does, however, identify a region within DP-178 beginning eight amino acids N-terminal to the start of 25 DP-178 and ending eight amino acids from the C- terminus. The DP-107 peptide has been shown experimentally to form a stable coiled coil. A search based on the Lupas search algorithm, therefore, would not have identified the DP-107 coiled-coil region.

Conversely, the Lupas algorithm identified the DP-178 30 region as a potential coiled-coil motif. However, the peptide DP-178 derived from this region failed to form a coiled coil in solution. A possible explanation for the inability of the Lupas search algorithm to accurately identify coiled-coil sequences within the 35 HIV-1 TM, is that the Lupas algorithm is based on the

structure of coiled coils from proteins that are not structurally or functionally similar to the TM proteins of viruses, antiviral peptides (e.g. DP-107 and DP-178) of which are an object of this invention.

5 The computer search strategy of the invention, as demonstrated in the Examples presented below, in Sections 9 through 16, successfully identifies regions of viral TM proteins similar to DP-107 or DP-178. This search strategy was designed to be used with a commercially-available sequence database packages, 10 preferably PC/Gene. A series of motifs were designed and engineered to range in stringency from very strict to very broad, as discussed in Section 9.

15 Among the protein sequence search motifs which may be utilized in such a computer-assisted DP-107-like and DP-178-like antiviral peptide search are the 107x178x4 motif, the ALLMOTI5 motif, and the PLZIP series of motifs, each of which is described in the Example presented in Section 9, below, with 107x178x4 being preferred.

20 Coiled-coiled sequences are thought to consist of heptad amino acid repeats. For ease of description, the amino acid positions within the heptad repeats are sometimes referred to as A through G, with the first position being A, the second B, etc. The motifs used 25 to identify DP-107-like and DP-178-like sequences herein are designed to specifically search for and identify such heptad repeats. In the descriptions of each of the motifs described, below, amino acids enclosed by brackets, i.e., [], designate the only 30 amino acid residues that are acceptable at the given position, while amino acids enclosed by braces, i.e., {}, designate the only amino acids which are unacceptable at the given heptad position. When a set of bracketed or braced amino acids is followed by a 35 number in parentheses i.e., (), it refers to the

number of subsequent amino acid positions for which the designated set of amino acids hold, e.g., a (2) means "for the next two heptad amino acid positions.

The ALLMOTI5 is written as follows:

5 {CDGHP]-{CFP}(2)-{CDGHP]-{CFP}(3)-
{CDGHP]-{CFP}(2)-{CDGHP]-{CFP}(3)-
{CDGHP]-{CFP}(2)-{CDGHP]-{CFP}(3)-
{CDGHP]-{CFP}(2)-{CDGHP]-{CFP}(3)-
{CDGHP]-{CFP}(2)-{CDGHP]-{CFP}(3)-

Translating this motif, it would read: "at the first (A) position of the heptad, any amino acid 10 residue except C, D, G, H, or P is acceptable, at the next two (B,C) amino acid positions, any amino acid residue except C, F, or P is acceptable, at the fourth heptad position (D), any amino acid residue except C, D, G, H, or P is acceptable, at the next three (E, F, 15 G) amino acid positions, any amino acid residue except C, F, or P is acceptable. This motif is designed to search for five consecutive heptad repeats (thus the repeat of the first line five times), meaning that it searches for 35-mer sized peptides. It may also be 20 designed to search for 28-mers, by only repeating the initial motif four times. With respect to the ALLMOTI5 motif, a 35-mer search is preferred. Those viral sequences identified via such an ALLMOTI5 motif are listed in Table V, below, at the end of this 25 Section. The viral sequences listed in Table V potentially exhibit antiviral activity, may be useful in the identification of antiviral compounds, and are intended to be within the scope of the invention.

The 107x178x4 motif is written as follows:

30 [EFIKLNQSTVWY]-{CFMP}(2)-[EFIKLNQSTVWY]-{CFMP}(3)-
[EFIKLNQSTVWY]-{CFMP}(2)-[EFIKLNQSTVWY]-{CFMP}(3)-
[EFIKLNQSTVWY]-{CFMP}(2)-[EFIKLNQSTVWY]-{CFMP}(3)-
[EFIKLNQSTVWY]-{CFMP}(2)-[EFIKLNQSTVWY]-{CFMP}(3)-

Translating this motif, it would read: "at the first (A) position of the heptad, any amino acid 35 residue except E, F, I, K, L, N, Q, S, T, V, W, or Y

is acceptable, at the next two (B,C) amino acid positions, any amino acid residue except C, F, M or P is acceptable, at the fourth position (D), any amino acid residue except E, F, I, K, L, N, Q, S, T, V, W, or Y is acceptable, at the next three (E, F, G) amino acid positions, any amino acid residue except C, F, M or P is acceptable. This motif is designed to search for four consecutive heptad repeats (thus the repeat of the first line four times), meaning that it searches for 28-mer sized peptides. It may also be designed to search for 35-mers, by repeating the initial motif five times. With respect to the 107x178x4 motif, a 28-mer search is preferred. Those viral sequences identified via such a 107x178x4 motif are listed in Table V, below, at the end of this Section. The viral sequences listed in Table V potentially exhibit antiviral activity, may be useful in the identification of antiviral compounds, and are intended to be within the scope of the invention.

The PLZIP series of motifs are as listed in FIG. 19. These motifs are designed to identify leucine zipper coiled-coil like heptads wherein at least one proline residue is present at some predefined distance N-terminal to the repeat. These PLZIP motifs find regions of proteins with similarities to HIV-1 DP-178 generally located just N-terminal to the transmembrane anchor. These motifs may be translated according to the same convention described above. Each line depicted in FIG. 19 represents a single, complete search motif. "X" in these motifs refers to any amino acid residue. In instances wherein a motif contains two numbers within parentheses, this refers to a variable number of amino acid residues. For example, X (1,12) is translated to "the next one to twelve amino acid residues, inclusive, may be any amino acid".

Tables VI through X, below, at the end of this

Section, list hits from such PLZIP motifs. The viral sequences listed in Table VI through X potentially exhibit antiviral activity, may be useful in the the identification of antiviral compounds, and are intended to be within the scope of the invention.

5 The Examples presented in Sections 17 and 18, below, demonstrate that respiratory syncytial virus and parainfluenza virus sequences identified via such a computer search exhibit antiviral and/or structural characteristics similar to those of DP-107 or DP-178.

10 The DP-107-like and DP-178-like analogous peptides may, further, contain any of the additional groups described for DP-178, above, in Section 5.1. For example, these peptides may include any of the additional amino-terminal groups which "X" of Tables I through IV may represent, and may also include any of the carboxy-terminal groups which "Z" of Tables I through IV may represent.

15 Additionally, such DP-107-like and DP-178-like peptides may furthr include DP-107-like or DP-178-like peptides, such as those listed in Tables V through X, above, containing one or more amino acid substitutions, insertions, and/or deletions. Also, analogs of such DP-107-like and DP-178-like peptides are intended to be within the scope of the invention.

20 25 Such analogs of the invention may exhibit increased antiviral activity, and may, further, posses increased bioavailability, and/or stability, or reduced immune recognition.

30 The DP-107-like and DP-178-like amino acid substitutions, insertions and deletions, are as described for DP-178, above, in Section 5.1. Analog modifications are as described, below, in Section 5.3.

TABLE V

Search Results Summary for 107x178x4 and
ALLMOTI5 Motifs

107X78X4	ALLMOT16
LIBRARY FILE	LIBRARY FILE
PENV_AVIRE	PENV1_FRSFV 341-376
PENV_AVIRE	PENV2_FRSFV 341-378
PENV_BAEVM	PENV_AVIRE 420-472
PENV_BIV06	PENV_AVISM 426-478
PENV_BIV27	PENV_BAEVM 390-468
PENV_BIVAF	PENV_BIV08 530-610 635-695
PENV_BIVAU	PENV_BIV27 558-639 684-724
PENV_BIVAV	PENV_BIVAF 304-379
PENV_BLV02	PENV_BLV/AU 304-379
PENV_BLV05	PENV_BLV/AV 304-379
PENV_BLVJ	PENV_BLV/B2 304-379
PENV_CAEVG	PENV_BLV/B5 304-379
PENV_EIAV1	PENV_BLVJ 304-379
PENV_EIAV2	PENV_CAEVC 157-186 615-720 761-785 847-895
PENV_EIAV3	PENV_CAEVG 154-183 613-718 749-783 846-893
PENV_EIAV5	PENV_EIAV1 436-525 569-593 688-716
PENV_EIAV9	PENV_EIAV2 436-525 569-593 688-692
PENV_EIAVC	PENV_EIAV3 438-526 569-593 688-716
PENV_EIAVW	PENV_EIAV5 437-526 560-594 689-693
PENV_EIAVY	PENV_EIAV8 438-525 569-593 688-716
PENV_FENV1	PENV_EIAVC 438-525 569-593 688-716
PENV_FIVPE	PENV_EIAVW 438-526 569-593 688-716
PENV_FIVSD	PENV_EIAVY 438-526 569-593 688-716
PENV_FIVT2	PENV_FENV1 503-555 687-804
PENV_FLYC8	PENV_FIVPE 610-880 715-759
PENV_FLYAL	PENV_FIVSD 801-888 713-754
PENV_FLYLB	PENV_FIVT2 808-889 714-765
PENV_FLYSA	PENV_FLYC8 497-549 681-695
PENV_FOAMV	PENV_FIVBL 478-530 642-676
PENV_FSVGA	PENV_FVBL 498-560 662-696
PENV_FSVGB	PENV_FVSA 476-527 539-573
PENV_FSVSM	PENV_FOAMV 321-365 563-693 888-903
PENV_GALV	PENV_FRSFB 318-364
PENV_HTLA	PENV_FSVGA 498-560 662-696
PENV_HTLIC	PENV_FSVGB 478-530 542-578
PENV_HTLIM	PENV_FSVSM 481-524 545-579
PENV_HTLV2	PENV_FSVST 498-532
PENV_HV1A2	PENV_GALV 523-576 687-821
PENV_HV1B1	PENV_HTLA 321-383
PENV_HV1B8	PENV_HTLIC 316-383
PENV_HV1BN	PENV_HTLIM 321-383
PENV_HV1BR	PENV_HTLV2 317-377
PENV_HV1C4	PENV_HV1A2 497-583 612-711 788-845
PENV_HV1EL	PENV_HV1B1 505-584 610-712 787-843
PENV_HV1H2	PENV_HV1B8 500-589 605-707 782-838

PENV_HV1H3	545-594	631-683	781-818		PENV_HV1BN	601-580	808-708	788-831	
PENV_HV1J3	558-605	642-694	802-829		PENV_HV1BR	610-588	615-717	772-841	
PENV_HV1JR	622-675	783-811			PENV_HV1C4	610-608	628-724	778-855	
PENV_HV1KB	565-598	637-677	776-824		PENV_HV1EL	602-581	807-708	788-829	
PENV_HV1MA	647-695	633-707	794-828		PENV_HV1H2	505-594	810-712	787-836	
PENV_HV1MF	643-692	629-681	789-816		PENV_HV1H3	505-594	810-712	787-843	
PENV_HV1MN	667-695	632-684	781-819		PENV_HV1J3	617-605	622-723	778-843	
PENV_HV1ND	636-683	621-673	783-813		PENV_HV1JR	497-588	803-704	758-835	
PENV_HV1QY	644-693	630-704	789-820		PENV_HV1KB	611-545	665-689	618-718	772-848
PENV_HV1PV	545-594	631-683	791-818		PENV_HV1MA	607-586	817-714	770-826	
PENV_HV1RH	554-602	640-692	800-832		PENV_HV1MF	603-592	822-710	786-841	
PENV_HV1S1	538-585	622-674	782-809		PENV_HV1MN	606-585	817-713	774-841	
PENV_HV1S3	541-689	627-679	787-815		PENV_HV1ND	495-584	801-702	757-825	
PENV_HV1SC	545-693	631-683			PENV_HV1QY	497-583	810-711	786-842	
PENV_HV1W1	645-693	631-683	781-818		PENV_HV1PV	505-584	810-712	787-843	
PENV_HV1W2	638-584	622-674	782-809		PENV_HV1RH	607-603	818-721	776-852	
PENV_HV1Z2	642-591	628-680	780-820		PENV_HV1S1	498-585	802-703	768-850	
PENV_HV1Z6	646-593	630-682	782-822		PENV_HV1S3	494-580	807-708	763-837	
PENV_HV1Z8	673-601	634-678	787-828		PENV_HV1SC	498-584	811-712	787-834	
PENV_HV1ZH	545-584	627-688	791-823		PENV_HV1W1	498-584	811-712	787-838	
PENV_HV2BE	532-591	621-648	653-697		PENV_HV1W2	489-584	802-703	768-827	
PENV_HV2CA	534-593	623-650	655-699		PENV_HV1Z2	502-581	807-708	784-831	
PENV_HV2D1	523-560	555-582	644-688		PENV_HV1Z8	504-583	808-711	788-840	
PENV_HV2G1	524-551	558-583	613-640	845-693	PENV_HV1ZB	612-601	817-675	682-718	774-831
PENV_HV2N2	524-551	556-583	613-640	662-689	PENV_HV1ZH	522-594	812-712	777-839	
PENV_HV2R0	533-682	622-688			PENV_HV2BE	510-585	817-680		
PENV_HV2S2	527-554	559-588	646-682		PENV_HV2CA	512-597	818-708		
PENV_HV2S8	567-684	614-673			PENV_HV2D1	501-586	808-698		
PENV_HV2ST	527-554	559-686	646-692		PENV_HV2G1	502-587	809-699		
PENV_MCF1	473-612				PENV_HV2N2	488-587	809-699		
PENV_MCF3	488-615				PENV_HV2R0	511-596	818-708		
PENV_MLVAV	517-644				PENV_HV2B2	505-580	812-702		
PENV_MLVCB	610-639				PENV_MCF1	473-588	814-700		
PENV_MLVF5	523-563				PENV_MCF3	474-526	538-572		
PENV_MLVFF	623-563				PENV_MLVAV	503-555	812-702		
PENV_MLVFP	623-563				PENV_IPMÆ	367-422	486-527		
PENV_MLVRD	497-538				PENV_JSRV	403-466	671-805		
PENV_MLVRK	497-538				PENV_MCF1	473-526	637-671		
PENV_MMTVB	458-485	562-689			PENV_MLVFS	520-584	573-610		
PENV_MMTVG	468-485	662-689			PENV_MLVFF	520-584	573-610		
PENV_MPMV	422-470				PENV_MLVHO	504-561	583-697		
PENV_MSVFB	67-84				PENV_MLVKI	40-92	104-138		
PENV_OMVVS	42-68	196-223	780-807		PENV_MLVMO	502-564	686-600		
PENV_RMCFV	487-517				PENV_MLVRD	497-549	661-695		

PENV SFV1	14-41	886-801			PENV MLVRK	497-549	581-595	
PENV SFV3L	18-45	319-357	873-700	883-898	PENV MMTRVB	477-539	558-612	
PENV SIVA1	601-588	692-619	652-879	697-724	PENV MMTRVG	477-539	558-612	
PENV SIVAG	688-683	687-824	658-685	703-730	PENV MPMV	408-474		
PENV SIVAI	548-603	634-708			PENV MSVFB	43-95	107-141	
PENV SIVAT	590-617	651-678			PENV QMVVS	22-84	185-223	684-748
PENV SIVAT	528-584	627-654			PENV RMCFV	484-528	640-674	
PENV SIVCZ	589-650	784-816			PENV RSFV	342-376		
PENV SIVGB	650-609	671-715			PENV SFV1	1-41	101-140	154-205
PENV SIVM1	650-609	671-715			PENV SFV3L	5-48	168-209	310-357
PENV SIVM2	168-216	277-289			PENV SIVAI	289-310	551-823	643-693
PENV SIVMK	663-608				PENV SIVAG	566-628	651-869	808-852
PENV SIVML	649-608				PENV SIVAI	257-291	336-370	535-607
PENV SIVS4	663-612	642-669	691-718		PENV SIVAT	284-298	545-821	644-892
PENV SIVSP	664-685	646-722			PENV SIVCZ	263-291	330-385	612-684
PENV SMRVH	400-482				PENV SIVGB	586-654	677-725	
PENV SRV1	408-471				PENV SIVM1	114-161	465-508	628-613
PENV VILV	773-600				PENV SIVM2	71-18	134-218	245-331
PENV VILV1	780-807				PENV SIVMK	484-505	640-612	638-724
PENV VILV2	782-809				PENV SIVML	484-505	640-612	638-724
PHEMA CVBLY	208-242				PENV VILV	21-62	184-222	638-809
PHEMA CVBM	208-242				PENV VILV1	21-62	184-222	643-748
PHEMA CVBQ	208-242				PENV VILV2	21-62	184-222	645-748
PHEMA CVHOC	208-242				PHEMA CVBLY	208-242		
PHEMA IAAIC	387-463				PHEMA CVBM	208-242		
PHEMA IABAN	371-437				PHEMA CVBQ	208-242		
PHEMA IABUD	381-451				PHEMA CVHOC	208-242		
PHEMA JACKA	381-451				PHEMA IAIC	380-458		
PHEMA JACKG	382-441	494-528			PHEMA IABAN	384-440		
PHEMA JACKP	398-426				PHEMA IABUD	378-454		
PHEMA JACKQ	398-426				PHEMA JACKA	378-454		
PHEMA JACKV	384-443				PHEMA JACKG	108-142	375-475	484-628
PHEMA IADA1	381-451				PHEMA IADA1	377-454		
PHEMA IADA2	423-463	499-543			PHEMA IADA2	377-476	485-537	
PHEMA IADA3	387-453				PHEMA IADA3	380-453		
PHEMA IADA4	418-478				PHEMA JACKS	377-469	504-549	
PHEMA IADC2	381-461				PHEMA JACKV	112-146	377-469	
PHEMA IADE1	402-453	508-533			PHEMA IADA4	377-454		
PHEMA IADH1	371-437				PHEMA IADC2	378-454		
PHEMA IADH2	371-437				PHEMA IADE1	21-55	377-472	
PHEMA IADH3	371-437				PHEMA IADH1	384-440		
PHEMA IADH4	371-437							
PHEMA IADH5	371-437							
PHEMA IADH6	371-437							
PHEMA IADH7	371-437							
PHEMA IADIR	416-446							
PHEMA IADM2	387-463							
PHEMA IADN2	381-461							

PHEMA_IADU3	387-453		PHEMA_IADH2	384-440
PHEMA_IAE7	387-453		PHEMA_IADH3	384-440
PHEMA_IAFPR	384-442		PHEMA_IADH4	384-440
PHEMA_IAGRE	381-461		PHEMA_IADH5	384-440
PHEMA_IAGU2	606-532		PHEMA_IADH6	384-440
PHEMA_IAGUA	604-631		PHEMA_IADH7	384-440
PHEMA_IAHAL	388-452		PHEMA_IADIR	379-471
PHEMA_IAHCS	388-457		PHEMA_IADM1	21-55
PHEMA_IAHCD	388-457		PHEMA_IADM2	380-456
PHEMA_IAHDE	388-457		PHEMA_IADNY	21-55
PHEMA_IAHFO	388-452		PHEMA_IADNZ	378-454
PHEMA_IAHK6	388-452		PHEMA_IADU1	21-55
PHEMA_IAHK7	388-452		PHEMA_IADU3	380-456
PHEMA_IAHLE	388-457		PHEMA_IADN7	380-456
PHEMA_IAHLO	388-457		PHEMA_IAFPR	377-477
PHEMA_IAHMI	388-452		PHEMA_IAGRE	378-454
PHEMA_IAHNM	388-452		PHEMA_IAGU2	378-473
PHEMA_IAHNN	388-457		PHEMA_IAGUA	377-478
PHEMA_IAHPR	388-457		PHEMA_IAHAL	379-455
PHEMA_IAHRO	388-452		PHEMA_IAHCB	112-148
PHEMA_IAHSA	388-452		PHEMA_IAHC7	112-148
PHEMA_IAHSP	388-457		PHEMA_IAHCD	380-484
PHEMA_IAHSW	388-457		PHEMA_IAHDE	380-484
PHEMA_IAHTE	388-452		PHEMA_IAHFO	379-456
PHEMA_IAHTO	388-455		PHEMA_IAHK6	378-456
PHEMA_IAHUR	388-452		PHEMA_IAHK7	379-456
PHEMA_IAKIE	425-478		PHEMA_IAHLE	112-148
PHEMA_IALEN	425-478		PHEMA_IAHLO	380-484
PHEMA_IAMAA	380-450		PHEMA_IAHMI	378-455
PHEMA_IAMAB	385-455		PHEMA_IAHNM	378-455
PHEMA_IAMAO	387-453		PHEMA_IAHNN	112-148
PHEMA_IAME1	387-453		PHEMA_IAHPR	380-484
PHEMA_IAME2	387-453		PHEMA_IAHRO	379-456
PHEMA_IAME6	371-437		PHEMA_IAHSA	378-455
PHEMA_IAMIN	382-441		PHEMA_IAHSP	112-148
PHEMA_IANT8	387-453		PHEMA_IASHW	380-484
PHEMA_IAPIL	605-534		PHEMA_IATHE	379-455
PHEMA_IAPUE	425-478		PHEMA_IATO	379-455
PHEMA_IARUD	381-451		PHEMA_IATHUR	378-455
PHEMA_IASE2	381-451		PHEMA_IAP	375-487
PHEMA_IASH2	508-547		PHEMA_IAKIE	378-478
PHEMA_IASTA	384-443		PHEMA_IALEN	378-478
PHEMA_IATKI	416-445		PHEMA_IAMAA	377-453
PHEMA_IATKM	381-461		PHEMA_IAMAB	382-458
PHEMA_IATKO	607-634		PHEMA_IAMAO	380-456
PHEMA_IATKP	424-454	493-639	PHEMA_IAME1	380-456
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PHEMA IATKR	381-422				PHEMA IAMES	384-440	
PHEMA IATKW	419-449	500-538			PHEMA IAMIN	108-142	375-476
PHEMA IAUDD	387-453				PHEMA IANT6	386-456	
PHEMA IAUSS	426-478				PHEMA IAPIL	378-477	488-534
PHEMA IAVI7	388-454				PHEMA IAPUE	378-478	508-548
PHEMA IAWIL	424-477				PHEMA IARUD	378-464	
PHEMA IAZCO	387-453				PHEMA IASB2	378-454	
PHEMA IAZH2	371-437				PHEMA IASH2	378-474	508-552
PHEMA IAZH3	371-437				PHEMA IASTA	112-148	377-469
PHEMA IAZIN	418-478	508-547			PHEMA IATK1	378-471	508-561
PHEMA IAZNJ	418-478	608-547			PHEMA IATKM	378-454	
PHEMA IAZUK	387-453				PHEMA IATKO	382-470	504-548
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PHEMA INBBO	390-421	428-473			PHEMA IATKR	30-84	374-474
PHEMA INBEN	398-428	427-481			PHEMA IATKW	373-472	487-539
PHEMA INBHK	391-418	428-473			PHEMA IATRA	21-65	
PHEMA INBLE	399-430	438-482			PHEMA IAUDO	387-456	
PHEMA INBMD	389-420	428-472			PHEMA IAUIS	376-478	508-548
PHEMA INBME	393-424	432-476			PHEMA IAV17	381-457	
PHEMA INBOR	398-428	437-481			PHEMA IAVIL	375-477	505-547
PHEMA INBSI	398-429	437-481			PHEMA IAZCO	380-458	
PHEMA INBUS	391-422	430-474			PHEMA IAZH2	384-440	
PHEMA INBV1	393-424	432-476			PHEMA IAZH3	384-440	
PHEMA INBVK	400-431	438-483			PHEMA IAZIN	379-478	508-548
PHEMA INCCA	496-571				PHEMA IAZNU	379-478	508-548
PHEMA INCEN	483-568				PHEMA IAZUK	380-456	
PHEMA INCGL	483-568				PHEMA INBEE	368-473	
PHEMA INCVK	482-568				PHEMA INBBO	378-463	
PHEMA INCJH	496-572				PHEMA INBEN	398-471	
PHEMA INCKY	492-568				PHEMA INBHK	381-463	
PHEMA INCMI	492-568				PHEMA INBIE	368-472	
PHEMA INCNA	482-568				PHEMA INBMD	377-482	
PHEMA INCP1	483-569				PHEMA INBME	381-468	
PHEMA INCP2	483-569				PHEMA INBOR	388-471	
PHEMA INCP3	483-569				PHEMA INBSI	388-471	
PHEMA INCTA	483-569				PHEMA INBUS	379-484	
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PHEMA NDVA	64-91				PHEMA INBVK	388-473	
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PHEMA NDVM	64-91				PHEMA INCJH	484-572	
PHEMA NDVQ	64-91				PHEMA INCKY	470-568	
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PHEMA_P13HA	27-61				PHEMA_INCYA	471-559
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PHEMA_P13HU	23-70				PHEMA_MEASH	48-80
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PHEMA_P13HW	27-61				PHEMA_MEASY	48-87
PHEMA_P13HX	27-61				PHEMA_MUMPM	34-98
PHEMA_RACV1	188-214	268-283			PHEMA_MUMPR	34-98
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PHEMA_SENDJ	78-108				PHEMA_NDVD	1-48
PHEMA_SENDZ	78-108				PHEMA_NDVM	1-48
PHEMA_S641	22-62	384-421			PHEMA_NDVQ	1-48
PHEMA_VACCC	118-148	175-202	216-243		PHEMA_NDVTG	1-48
PHEMA_VACCI	108-148	175-202	216-243		PHEMA_NDVU	1-48
PHEMA_VACCT	118-148	175-202	216-243		PHEMA_PHODV	38-73
PHEMA_VACCV	108-148	175-202	216-242		PHEMA_P11HW	88-110
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PVF11_VACCC	274-321				PHEMA_P13HV	13-110
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PVF12_VACCC	10-37	113-140	654-681		PHEMA_P13HX	13-110
PVF12_VACCP	10-37	113-140	654-681		PHEMA_P14HA	64-88
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PVGO5_VACCC	48-76	131-161	226-289	366-389	PVENV_MCV1	262-286
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PV0309_VARV	308-338				PV0309_VACCP	257-295			
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PV031_SPV1R	280-287				PV03 VACCC	71-110			
PV031_SPV4	287-314	383-410			PV03 VACCV	71-110			
PV0322_HSV1	373-400	681-692	688-705	768-824	PV05 VACCC	81-129	282-320		
PV0324_HSV1	31-58				PV05 VACCP	81-128	282-320		
PV0328_HSV1	263-280	497-568			PV05 VACCV	81-128	282-321		
PV0329_ANEPV	33-84	91-118			PV11_VACCC	217-268	288-316		
PV0329_SPV1R	285-326				PV11_VACCP	213-254	265-311		
PV0329_SPV4	148-173	175-205	282-310		PV12_VACCC	1-67	102-143	198-238	350-388
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PVGL2 IBVB	808-835	876-902	1058-1080	PVG37 HSV1	435-472		
PVGL2 IBVD2	809-836	876-903	1057-1081	PVG38 HSV1	84-118		
PVGL2 IBVK	808-835	875-902	1058-1080	PVG39 HSV1	124-158	288-300	
PVGL2 IBVM	608-836	876-902	1056-1080	PVG3 SPV1R	8-49	162-186	203-214
PVGLB EBV	95-122	631-658		PVG3 SPV4	8-54	87-121	
PVGLB HCMVA	26-88	387-424	440-487	PVG43 HSV1	116-150	262-298	324-361
PVGLB HCMVT	50-88	387-424	435-482	PVG45 HSVSA	121-162		
PVGLB HSVB1	427-454			PVG46 HSV1	45-88	939-1078	1251-1321
PVGLB HSVB2	447-474			PVG48 HSV1	189-207		
PVGLB HSVBC	428-453			PVG48 HSVSA	380-417	611-666	733-767
PVGLB HSVE1	443-470	934-981		PVG49 HSVSA	68-102		
PVGLB HSVE4	488-513	816-843		PVG4R AMEPV	4-38		
PVGLB HSVEA	443-470	934-961		PVG4 SPV4	89-130		
PVGLB HSVEB	443-470	934-961		PVG51 HSV1	34-73	89-123	
PVGLB HSVEL	443-470	933-960		PVG51 HSVSA	29-70	123-167	162-186
PVGLB HSVMD	93-120	352-378		PVG53 HSV1	67-127		
PVGLB MCMVS	381-408	441-476		PVG54 HSV1	356-388		
PVGLC HSV11	469-510			PVG55 HSV1	101-135		
PVGLC HSV1K	469-510			PVG55 HSVSA	126-178		
PVGLC HSVFB	124-151			PVG66 HSV1	151-192	678-912	644-878
PVGLC HSVMB	63-87			PVG68 HSV1	10-72	88-123	
PVGLC HSVMG	62-88			PVG69 HSVSA	189-209		
PVGLC HSVMM	63-97			PVG6 SPV1R	85-103		
PVGLC VZVD	286-322			PVG81 HSV1	285-299		
PVGLC VZVS				PVG83 HSV1	546-584		
PVGLF HSV2	111-148			PVG65 HSV1	806-839	1213-1254	
PVGLF HSMQ	38-65	154-202	216-243	PVG66 HSV1	154-188	328-410	
PVGLF HSMVM	38-65	154-202	216-243	PVG67 HSV1	378-413	601-546	1321-1368
PVGLF BRSV/C	38-65	154-202	216-243	444-471	488-533	PVG68 HSV1	245-288
PVGLF BRSV/R	285-322			PVG72 HSV1	447-484	723-767	812-949
PVGLF CDVO	252-293	340-367		PVG75 HSV1	271-305	388-422	
PVGLF HRSV1	38-65	154-203	442-471	488-516		PVG8 SPV1R	5-51
PVGLF HRSV/A	38-65	154-202	213-243	488-518		PVG1 HSVB	142-178
PVGLF HRSVL	38-65	154-202	216-243	444-471	488-516	PVG1 HSVB	1233-1267
PVGLF HRSVR	38-65	154-202	213-243	442-471	488-518	PVG3 HSVVA	10-44
PVGLF MEASE	228-262					PVGL2 CVBF	842-878
PVGLF MEASI	231-285					PVGL2 CVBL9	850-885
							903-1108
							1263-1305

PVGIF MEASY	228-282			PVGIF2_CVBLY	642-876	866-886	883-1108	1233-1306	
PVGIF MUMPM	20-54	447-488		PVGIF2_CVBM	642-878	866-886	883-1108	1233-1305	
PVGIF MUMPR	20-54	447-488		PVGIF2_CVHQ	642-878	866-885	883-1108	1233-1305	
PVGIF MUMPS	161-178	426-511		PVGIF2_CVIV	642-878	866-885	883-1108	1233-1305	
PVGIF NDVA	161-178	426-512		PVGIF2_CVH22	770-916	1055-1112			
PVGIF NDVB	161-178	426-512		PVGIF2_CVIM4	643-884	1001-1117	1270-1315		
PVGIF NDVI	161-178	426-512		PVGIF2_CVIM5	691-932	949-1079	1218-1263		
PVGIF NDVM	161-178	426-512		PVGIF2_CVIMH	602-543	866-976	1129-1174		
PVGIF NDVT	161-178	426-512		PVGIF2_CVPPS	69-110	446-482	692-733	886-923	1040-1186
PVGIF NDVTG	161-178	426-512		PVGIF2_CVPPU	69-110	446-480	680-731	887-921	1038-1184
PVGIF NDVU	161-178	426-512		PVGIF2_CVPR8	224-268	408-509	665-889	816-952	1128-1166
PVGIF PHODV	36-63	221-282	309-338	PVGIF2_CVPRM	224-268	486-508	665-888	816-952	1128-1165
PVGIF PI1HC	147-174	210-286		PVGIF2_EBV	68-102				
PVGIF PI2H	80-117	141-175	238-286	PVGIF2_FIPV	188-245	451-485	695-738	892-928	1043-1188
PVGIF PI2HQ	80-117	141-175	238-286	PVGIF2_IBV8	791-905	1057-1091			
PVGIF PI2HT	80-117	141-176	238-288	PVGIF2_IBVB	437-478	772-904	1056-1080		
PVGIF PI3B	115-182	207-241	458-497	PVGIF2_IBVD2	773-905	1057-1091			
PVGIF PI3H4	115-182	207-241	457-497	PVGIF2_IBVK	437-478	772-904	1056-1080		
PVGIF RINDK	224-285	458-486		PVGIF2_IBVM	437-478	772-904	1056-1080		
PVGIF RINDL	224-285	468-508		PVGIF2_HCMVA	438-88	128-162	436-484	844-878	
PVGIF SEND6	122-149	211-245	480-507	PVGIF2_HCMVT	22-88	128-162	437-485	845-879	
PVGIF SENDF	122-149	211-245	480-507	PVGIF2_HSV11	828-880				
PVGIF SENDH	122-149	211-245	480-507	PVGIF2_HSV1F	827-889				
PVGIF SENDJ	122-149	211-245	480-507	PVGIF2_HSV1K	827-889				
PVGIF SENDZ	122-149	211-245	480-507	PVGIF2_HSV1P	828-890				
PVGIF SV41	144-185	241-269	459-486	PVGIF2_HSV23	828-890				
PVGIF SV5	137-171	417-444		PVGIF2_HSV2H	828-890				
PVGIF TRTV	124-161	193-200	457-484	PVGIF2_HSV2S	617-871	185-223			
PVGIF BFFV	623-557			PVGIF2_HSV6U	37-71				
PVGIF BRSVC	92-123			PVGIF2_HSVB1	859-913				
PVGIF HRSV1	63-93			PVGIF2_HSVB2	440-474	848-902			
PVGIF HRSV4	68-107			PVGIF2_HSVBC	883-900				
PVGIF HRSV5	243-273			PVGIF2_HSVE1	542-576	911-961			
PVGIF HRSV8	68-93			PVGIF2_HSVE4	474-515	847-900			
PVGIF HSVE4	271-288			PVGIF2_HSVEA	542-576	911-961			
PVGIF HSVEB	383-410			PVGIF2_HSVEB	542-576	911-961			
PVGIF RABVT	489-518			PVGIF2_HSVEL	642-578	910-960			
PVGIF VSV1G	472-489			PVGIF2_VZVD	92-133	596-630	808-867		
PVGIF EBV	549-578	618-648		PVGIF2_HSVM	380-435	648-883	787-945		
PVGIF HCMVA	107-138	270-287		PVGIF2_HSVA	240-288	406-447			
PVGIF HCMVT	108-135			PVGIF2_MCMVB	208-280	427-476	693-778	860-894	
PVGIF HSV6G	62-89	380-403		PVGIF2_PRVIF	847-881				
PVGIF HSVSA	388-416								
PVGIF HCMVA	47-111								
PVGIF BUNGE	612-646	614-641	1128-1266	PVGIF2_HSV2	442-476				
PVGIF BUNL7	813-980			PVGIF2_HSV23	443-477				
PVGIF BUNYW	340-374	604-636	682-708	PVGIF2_HSVBC	236-289				

PVGLM_DUGBV	845-972			PVGLC_HSVEB	182-218	
PVGLM_HANTB	73-100	683-720		PVGLC_HSVMB	63-87	
PVGLM_HANTH	75-102			PVGLC_HSVMG	62-88	
PVGLM_HANTL	76-102			PVGLC_HSVMM	63-87	
PVGLM_HANTV	76-102			PVGLC_PRVIF	183-235	
PVGLM_PHV	69-86			PVGLC_V2VD	280-321	
PVGLM_PUOMH	72-110			PVGLC_V2VS	280-321	
PVGLM_PUOMS	72-110			PVGLD_HSVEA	89-123	
PVGLM_SEOUR	73-100	613-540	884-721	PVGLD_HSVEB	139-173	
PVGLM_SEOUS	73-100	613-540	884-721	PVGLD_HSVEK	139-173	
PVGLN_BEFV	523-564			PVGLE_HSV11	111-145	
PVGLP_BEV	48-82	1145-1179	1184-1211	15056-1632	PVGLE_HS2	111-168
PVGLX_HSVEB	17-44	413-444		PVGLF_BRSVA	146-202	504-546
PVGLX_PRVRI	427-461			PVGLF_BRSVC	146-202	287-302
PVGLY_JUNIN	14-41			PVGLF_BRSVR	146-202	287-302
PVGLY_LASSQ	88-113			PVGLF_CDVO	228-287	340-381
PVGLY_MOPEI	86-113	316-348		PVGLF_HRSV1	118-203	287-302
PVGLY_PIARV	334-376			PVGLF_HRSVA	118-202	287-302
PVGLY_TACV	109-138	316-360		PVGLF_HRSVL	118-202	287-302
PVGLY_TACV6	303-338			PVGLF_HRSVR	118-202	287-302
PVGLY_TACV7	302-337			PVGLF_MEASE	118-184	228-268
PVGLY_TACVT	303-338			PVGLF_MEASI	118-187	231-272
PVGLZ_HSVEK	17-44			PVGLF_MEASY	118-184	228-269
PVGLM_BPMV	403-430			PVGLF_MLMFM	20-54	103-179
PVGLM_CPSMV	192-221			PVGLF_MLMFR	20-54	103-179
PVGLB_EBV	104-149			PVGLF_MLMPS	20-54	103-178
PVMA1_Reovl	280-317			PVGLF_NDAV	117-182	231-272
PVMA11_Reovd	625-882			PVGLF_NDB	122-182	231-272
PVMA22_Reovd	624-861			PVGLF_NDI	133-182	238-272
PVMA2_Reovj	824-861			PVGLF_NDM	117-182	231-272
PVMA3_Reovd	169-188	343-370	466-493	631-880	PVGLF_NDT	117-182
PVMA2_BREVA	124-162			PVGLF_NDTG	122-182	231-272
PVMA2_HRSVA	124-161			PVGLF_NDU	122-182	231-272
PVMA1_BREVA	219-248			PVGLF_PHODV	28-63	187-266
PVMA1_HRSVA	219-248			PVGLF_P1HC	123-174	207-267
PVMA1_INCJJ	161-186			PVGLF_P12H	93-183	477-528
PVMA1_HDVA	247-274			PVGLF_P12HG	93-183	477-528
PVMA1_P12HT	98-123			PVGLF_P12HT	93-185	477-528
PVMA1_P13B	201-231			PVGLF_P13B	117-182	207-241
PVMA1_P13H4	201-231			PVGLF_P13H4	117-182	207-241
PVMA1_SV41	323-363			PVGLF_RINDK	112-180	224-266
PVME1_CVBM	175-209			PVGLF_RINDL	112-180	224-266
PVME1_CVTKE	175-209			PVGLF_SEND5	127-188	211-271
PVME1_IBV8	21-48	184-218		PVGLF_SENDF	127-188	211-271
PVME1_IBVB	21-48	184-218		PVGLF_SENDH	127-188	218-271
PVME1_IBVB2	21-48	184-218		PVGLF_SENDJ	127-188	211-271
PVME1_IBVK	184-218			PVGLF_SENDZ	127-188	211-271

PVMP CAMVC	220-264	273-324	PVGLF SV/41	98-188	454-508
PVMP CAMVD	28-58	220-264	PVGLF SV/5	103-71	241-275
PVMP CAMVE		227-254	PVGLF TRIV	105-161	180-224
PVMP CAMVN		220-254	PVGLG BFRV	508-812	457-498
PVMP CAMVS		220-254	PVGLG BR9VC	30-70	104-138
PVMP CAMVW		220-254	PVGLG HRSV1	30-81	
PVMP CERV	26-53	100-127	PVGLG HRSV2	30-85	
PVMP SOCMV	4-31	78-118	PVGLG HRSV3	30-85	
PVMSA HPBHE	294-328		PVGLG HRSV4	30-107	
PVMT1 DHV11	38-65	237-284	PVGLG HRSV5	30-85	
PVMT8 MYXVL	163-180		PVGLG HRSV6	30-85	
PVMT9 MYXVL	485-492		PVGLG HRSV7	30-85	
			PVGLG HRSV8	30-81	
			PVGLG HRSV9	30-87	
			PVGLG HRSVL	25-85	
			PVGLG HSV4	271-305	
			PVGLG SIGMA	344-381	484-498
			PVGLG SY/NV	488-523	
			PVGLG VHSV0	393-397	
			PVGLG VSVIG	476-510	
			PVGLH EEV	83-87	180-201
			PVGLH HCMVA	103-137	270-311
			PVGLH HCMVLT	102-136	692-740
			PVGLH HSV11	447-481	
			PVGLH HSV1E	447-481	
			PVGLH HSV8G	357-408	
			PVGLH HSVBC	364-416	
			PVGLH HSVE4	334-379	414-455
			PVGLH HVEB	327-372	407-448
			PVGLH HSVSA	322-68	374-453
			PVGLH MCMVS	440-474	
			PVGLH PRVKA	228-280	
			PVGLH PRVN3	228-280	
			PVGLH PRVRI	228-280	
			PVGLH VZD	456-508	
			PVGLI HCMVA	47-111	323-359
			PVGLM BUNGE	612-587	685-737
			PVGLM_BUNL7	643-877	918-950
			PVGLM_BUNSH	643-877	
			PVGLM_BUNW	340-374	504-563
			PVGLM_DUBV	937-989	1238-1300
			PVGLM_HANTB	683-727	
			PVGLM_HANTH	72-106	
			PVGLM_HANTL	72-106	
			PVGLM_HANTV	72-106	
			PVGLM_PHV	73-111	
			PVGLM_PTPV	149-251	

PVGLM_SEOUR	694-728
PVGLM_SEOUS	693-730
PVGLN_BEFV	377-414
PVGLP_BEV	43-82
PVGLX_HSVEB	177-262
PVGLX_PRVRI	420-461
PVGLY_JUNIN	301-349
PVGLY_LASSA	317-380
PVGLY_LASSJ	318-381
PVGLY_LYCVIA	333-387
PVGLY_LYCVW	124-168
PVGLY_MOPEI	318-369
PVGLY_PIARV	334-375
PVGLY_TACV	316-383
PVGLY_TACV6	303-361
PVGLY_TACV7	302-360
PVGLY_TACVT	303-361
PVGNB_CPMV	835-888
PVGNM_BPMV	143-177
PVGNM_CPMV	160-201
PVGNM_CPMV	192-228
PVGNM_RCMV	837-871
PVGP8_EBV	94-149
PVNO1_VACCC	5-56
PVM1_RECVL	287-321
PVM21_RECVD	418-450
PVM22_RECVD	418-450
PVM2_RECVJ	418-450
PVM2_RECVL	418-450
PVM3_RECVD	135-180
PVM42_BPSVA	4-90
PVM42_HPSVA	4-2-80
PVMAT_CDV0	183-234
PVMAT_INCJJ	73-114
PVMAT_NOVA	310-368
PVMAT_NOVB	324-386
PVMAT_PISB	98-133
PVMAT_PISI4	98-133
PVMAT_RABVA	69-103
PVMAT_RABVC	69-103
PVMAT_RABVE	69-103
PVMAT_RABVN	69-103
PVMAT_RABVP	69-103
PVMAT_RABVS	69-103
PVMAT_SYN	248-280
PVMAT_VSVIG	188-232
PVME1_CVBM	175-208

PVME1_CVPPFS	98-148	212-267
PVME1_CVPPU	212-267	
PVME1_CVPRM	212-267	
PVME1_CVTKE	28-62	176-208
PVME1_FIPV	212-267	
PVME1_IBV8	21-56	177-218
PVME1_IBV8	21-56	177-218
PVME1_IBV2	21-56	177-218
PVME1_IBVK	38-94	
PVMP_CAMVGC	187-264	270-324
PVMP_CAMVGD	187-264	270-324
PVMP_CAMVE	187-264	270-324
PVMP_CAMVN	187-264	270-324
PVMP_CAMVB	187-264	270-324
PVMP_CAMVN	187-264	270-324
PVMP_CERFV	212-248	
PVMP_FWVD	217-261	
PVMP_SOCMV	76-118	
PVMSA_HPBDB	272-313	324-361
PVMSA_HPBDC	271-312	323-360
PVMSA_HPBDU	234-276	289-323
PVMSA_HBBDW	272-313	324-361
PVMSA_HBBS	210-244	
PVMSA_HBBHE	284-328	
PVMSA_WHV1	208-242	
PVMSA_WHV58	213-247	
PVMSA_WHV7	213-247	
PVMSA_WHV8I	213-247	
PVMT1_D4V1	201-235	
PVMT1_IANN	82-126	174-222
PVMT1_JABAN	82-126	174-222
PVMT1_IACAO	31-78	
PVMT1_IAFOW	82-126	174-222
PVMT1_IAPPR	82-126	174-222
PVMT1_IAPPV	82-126	174-222
PVMT1_IALE1	82-126	174-222
PVMT1_IALE2	82-126	174-222
PVMT1_IAMAN	82-126	174-222
PVMT1_IAPOC	82-126	174-222
PVMT1_IAPUE	82-126	174-222
PVMT1_IAUDIO	82-126	174-222
PVMT1_IAVIL	82-126	174-222
PVMT1_IAZI1	92-126	174-222
PVMT1_INBAC	176-209	
PVMT1_INBAD	176-209	
PVMT1_INBLE	176-209	
PVMT1_INBSI	176-209	

PV/MT2	INBAC	132-184
PV/MT2	INBAD	132-184
PV/MT2	INBLE	132-184
PV/MT2	INBSI	132-184
PV/MT8	MT7VL	46-80
		145-187

TABLE VI

Search Results Summary for PCTLZIP,
P1CTLZIP, and P2CTLZIP Motifs

PCT ZIP	P1CTLZIP	P2CTLZIP			
LIBRARY FILE	LIBRARY FILE	LIBRARY FILE			
PENV FOAMV	481-486	PENV BIV08	434-460	PENV BIV06	525-542
PENV HV1MA	438-453	PENV BIV27	463-478	PENV BIV27	554-571
PENV HV1MF	183-198	PENV FOAMV	481-498	PENV FENV1	30-47
PENV HV1RH	445-450	PENV HV1KB	762-768	PENV FIVPE	781-798
PENV HV1SC	186-201	PENV HV1MA	497-493	PENV FIVSD	778-798
PENV HV122	123-138	PENV HV1MF	183-198	PENV FIVT2	780-797
PENV HV12H	438-453	PENV HV1RH	444-460	PENV FLVC8	38-56
PENV HV2BE	750-765	PENV HV151	758-764	PENV FLVGL	605-622
PENV HV2D1	741-756	PENV HV13C	188-201	PENV FLVLB	825-842
PENV HV2G1	741-756	PENV HV122	123-138	PENV FLVSA	802-818
PENV HV2NZ	742-757	PENV HV123	117-133	PENV FOAMV	710-727
PENV HV2RO	751-766	PENV HV12H	437-453	PENV FSVGA	825-842
PENV HV2SB	743-758	PENV HV2BE	760-765	PENV FSVGB	605-622
PENV HV2ST	746-760	PENV HV2D1	741-756	PENV FSVSM	608-625
PENV JSRV	104-118	PENV HV231	741-756	PENV HV1OY	123-140
PENV MMTVB	818-833	PENV HV2N2	742-757	PENV HV122	410-427
PENV MMTVG	818-833	PENV HV2R0	751-766	PENV HV1Z3	154-171
PENV SIVMK	138-154	PENV HV2S8	743-758	PENV HV2CA	760-767
PENV SIVML	138-154	PENV HV2ST	745-760	PENV MCFF	600-617
PHEMA CVBLY	391-408	PENV JSRV	104-119	PENV MCFF3	601-618
PHEMA CVBM	391-408	PENV MCFF	307-413	PENV MLVAV	630-647
PHEMA CVBQ	391-408	PENV MCFF3	307-413	PENV MLVCB	825-842
PHEMA CVHOC	391-408	PENV MLVAV	427-443	PENV MLVFB	839-868
PHEMA CVMA6	402-417	PENV MLVCB	422-438	PENV MLVFF	839-868
PHEMA CVMS	403-418	PENV MLVHO	423-438	PENV MLVFP	839-868
PHEMA INBAA	288-310	PENV MLVMO	428-442	PENV MLVHO	826-843
PHEMA INBBE	303-318	PENV MLVRD	434-440	PENV MLVJK	187-184
PHEMA INBBO	283-308	PENV MLVRK	424-440	PENV MLVMO	829-846
PHEMA INBEN	301-318	PENV MMIVB	618-633	PENV MLVRD	824-841
PHEMA INBFU	288-301	PENV MMIVG	818-833	PENV MLVRK	824-841
PHEMA INBGL	288-311	PENV SFV1	884-880	PENV MSVFB	170-187
PHEMA INBHK	283-308	PENV SFV2L	861-877	PENV RMCFV	603-620
PHEMA INBIB	288-303	PENV SIVGB	93-109	PENV SFV1	710-727
PHEMA INBID	288-314	PENV SIVMK	139-154	PENV SFV3L	707-724
PHEMA INBLE	302-317	PENV SIVML	139-154	PENV SIVM1	768-783
PHEMA INBMD	282-307	PENV SIVS4	808-822	PENV SIVMK	765-782
PHEMA INBME	288-311	PENV SIVSP	810-826	PENV SIVML	764-781
PHEMA INBNA	288-303	PHEMA CDVO	36-52	PENV SIVS4	768-788
PHEMA INBOR	301-316	PHEMA CVBLY	381-408	PENV SIVSP	773-790
PHEMA INBSI	301-316	PHEMA CVBM	381-408	PENV SMRVM	638-653
PHEMA INBSJ	298-313	PHEMA CVBQ	381-408	PENV SMSAV	42-58
PHEMA INBJS	294-309	PHEMA CVHOC	381-408	PHEMA CDVO	38-53
PHEMA INBVI	288-311	PHEMA CVMA6	402-417	PHEMA CVBLY	391-408
PHEMA INBVK	303-318	PHEMA CVMS	403-418	PHEMA CVBM	391-408
PHEMA INBYB	288-301	PHEMA IAIIC	237-253	PHEMA CVBQ	391-408

PHEMA_MUMPR	133-148	PHEMA_IABAN	221-237				PHEMA_CVHOC	381-408
PHEMA_MUMPR	133-148	PHEMA_IABUD	234-250				PHEMA_IAAIC	322-339
PHEMA_MUMPS	133-148	PHEMA_IACKA	234-250				PHEMA_IABAN	308-323
PHEMA_P11HW	345-360	PHEMA_IACKG	231-247				PHEMA_IABUD	320-337
PHEMA_P12H	65-80	PHEMA_IACKV	230-246				PHEMA_IACKA	320-337
PHEMA_P12HT	65-80	PHEMA_IADA1	234-250				PHEMA_IACKG	316-333
PHEMA_RINDK	368-383	PHEMA_IADA3	237-253				PHEMA_IACKP	302-319
PHEMA_SVS	7-94	PHEMA_IADCZ	234-250				PHEMA_IACKQ	302-319
PHEMA_SV5CM	7-94	PHEMA_IADI1	221-237				PHEMA_IACKS	318-336
PHEMA_SV5CP	7-94	PHEMA_IADI2	221-237				PHEMA_IACKV	315-332
PHEMA_SV5IN	7-94	PHEMA_IADI3	221-237				PHEMA_IADA1	320-337
PVENV_DHV11	42-57	PHEMA_IADI4	221-237				PHEMA_IADA3	322-339
PVF7_CAPVK	88-104	PHEMA_IADI5	221-237				PHEMA_IADCZ	320-337
PVF8_VACC8	72-87	PHEMA_IADI6	221-237				PHEMA_IADH1	308-323
PVG01_BPP22	242-257	PHEMA_IADI7	221-237				PHEMA_IADH2	308-323
PVG01_HSVEB	168-184	PHEMA_IADM2	237-253				PHEMA_IADH3	308-323
PVG01_HSV11	210-225	317-332	PHEMA_IADN2	234-250			PHEMA_IADH4	320-337
PVG08_BPT4	184-198	PHEMA_IAEN8	221-237				PHEMA_IADH6	308-323
PVG07_BPT4	885-900	PHEMA_IAEN7	237-253				PHEMA_IADH7	308-323
PVG08_HSV11	134-149	PHEMA_IAPPR	230-246				PHEMA_IADN2	322-339
PVG10_BPPH2	183-198	PHEMA_IAHAL	238-262				PHEMA_IADNZ	320-337
PVG10_BPPZA	183-198	PHEMA_IAHAR	236-261				PHEMA_IADU3	322-339
PVG10_HSVSA	109-124	PHEMA_IAHC8	230-246				PHEMA_IAE6	308-323
PVG16_BPP1	81-98	PHEMA_IAHC7	230-246				PHEMA_IAE7	322-339
PVG18_BPT4	466-483	PHEMA_IAHCD	230-246				PHEMA_IAFPR	315-332
PVG25_BPT4	87-112	PHEMA_IAHDE	230-246				PHEMA_IAGRE	320-337
PVG29_HSV11	20-35	PHEMA_IAHFO	236-262				PHEMA_IAGU2	320-337
PVG30_BPPH8	11-84	PHEMA_IAK8	236-262				PHEMA_IAGUA	318-336
PVG36_BPOX2	22-37	PHEMA_IAK7	236-262				PHEMA_IAHAL	321-338
PVG36_HSVSA	108-123	PHEMA_IAHLE	230-246				PHEMA_IAHCB	315-332
PVG37_BPT2	1263-1268	PHEMA_IAHLO	230-246				PHEMA_IAHC7	315-332
PVG37_HSV11	284-289	PHEMA_IAHMI	236-252				PHEMA_IAHCD	315-332
PVG65_HSV11	22-37	143-168	PHEMA_IAHNM	236-252			PHEMA_IAHDE	315-332
PVG68_HSV11	268-283	PHEMA_IAHRO	236-252				PHEMA_IAHFO	321-338
PVG68_HSV11	102-117	PHEMA_IAHSA	236-252				PHEMA_IAHK8	321-338
PVG69_HSV11	267-282	PHEMA_IAHSP	230-246				PHEMA_IAHK7	321-338
PVG69_HSV11	518-533	PHEMA_IASHW	230-246				PHEMA_IAHLE	315-332
PVG9_BPPH2	234-249	PHEMA_IAHTE	236-262				PHEMA_IAHLO	315-332
PVG9_BPPZA	234-249	PHEMA_IAHTO	236-262				PHEMA_IAHMI	321-338
PVG9_BPVIR	67-72	PHEMA_IAHUR	236-252				PHEMA_IAHNM	321-338
PVGf_BPPHX	234-249	PHEMA_IAKIE	235-251				PHEMA_IAHNN	315-332
PVG2_CVBF	264-278	PHEMA_IALEN	235-251				PHEMA_IAHPR	315-332
PVG2_CVBL9	264-279	PHEMA_IAMAA	233-249				PHEMA_IAHRO	321-338
PVG2_CVBLY	284-279	PHEMA_IAMAB	238-264				PHEMA_IAHSA	321-338
PVG2_CVBM	284-279	PHEMA_IAMAO	237-263				PHEMA_IAHSP	315-332
PVG2_CVBR	284-279	PHEMA_IAME1	237-263				PHEMA_IAHSW	315-332
PVG2_CVBY	284-279	PHEMA_IAME2	237-263				PHEMA_IAHTE	321-338

PV/QL2_CVPPS	442-457	PHEMA_IAME6	221-237		PHEMA_IAHTO	321-338
PV/QL2_CVPPU	440-455	504-519	PHEMA_IAMIN	85-101	PHEMA_IAHUR	321-338
PV/QL2_CVPRB	218-233	PHEMA_IANT8	231-253		PHEMA_IAJAP	317-334
PV/QL2_CVPRM	218-233	PHEMA_IACU7	221-237		PHEMA_IANAA	319-336
PV/QL2_IBV6	1056-1071	PHEMA_IARUD	231-250		PHEMA_IAMAB	324-341
PV/QL2_IBVB	1055-1070	PHEMA_IASE2	231-250		PHEMA_IAMAO	322-339
PV/QL2_IBD2	1066-1071	PHEMA_IASH12	234-250		PHEMA_IAME1	322-339
PV/QL2_IBVX	1055-1070	PHEMA_IASTA	230-248		PHEMA_IAME2	322-339
PV/QL2_IBVM	1055-1070	PHEMA_IATAI	235-251		PHEMA_IAME6	306-323
PV/QLB_HS/SA	701-716	PHEMA_IATKM	234-250		PHEMA_IAMIN	316-333
PV/QLB_PRVIF	203-218	PHEMA_IATKO	233-249		PHEMA_IANT6	322-339
PV/QLC_HSVBC	475-490	PHEMA_IATKR	230-246		PHEMA_IAPIL	320-337
PV/QLC_HS/VE4	444-459	PHEMA_IATKW	228-246		PHEMA_IAQUT	306-323
PV/QLC_HS/VEB	427-442	PHEMA_IAUDO	231-253		PHEMA_IARUD	320-337
PV/QLC_PRVIF	446-461	PHEMA_IAUSS	235-251		PHEMA_IASE2	320-337
PV/QLD_HSV11	78-94	PHEMA_IAV17	238-254		PHEMA_IASH2	321-338
PV/QLD_HSV2	78-94	PHEMA_IAXIA	235-261		PHEMA_IASTA	315-332
PV/QLF_BR/VA	285-280	PHEMA_IACZCO	231-253		PHEMA_IATKM	320-337
PV/QLF_BR/VC	265-280	PHEMA_IAZH12	221-237		PHEMA_IAUDIO	322-339
PV/QLF_BR/VR	285-280	PHEMA_IAZH13	221-237		PHEMA_IAV17	323-340
PV/QLF_HR/8V1	285-280	PHEMA_IAZH14	237-253		PHEMA_IAZCO	322-339
PV/QLF_HR/8VA	265-280	PHEMA_INBALA	118-131	285-310	PHEMA_IAZH2	306-323
PV/QLF_HR/8VL	265-280	PHEMA_INBEE	123-139	303-318	PHEMA_IAZH3	306-323
PV/QLF_HR/8VR	265-280	PHEMA_INBEO	118-132	283-308	PHEMA_IAZUK	322-339
PV/QLF_NUMPS	5-94	PHEMA_INBEN	123-138	301-316	PHEMA_MUMPM	101-118
PV/QLI_VZ/0	278-293	PHEMA_INBEU	108-124	286-301	PHEMA_MUMPR	101-118
PV/QLM_HANTB	900-915	PHEMA_INBGL	118-135	286-311	PHEMA_MUMPS	101-118
PV/QLM_PTPV	743-758	PHEMA_INBHK	118-132	283-308	PHEMA_NDVA	93-110
PV/QLM_SEOUR	901-916	PHEMA_INBIB	108-124	288-303	PHEMA_NDVM	93-110
PV/QLM_SEOUS	900-915	PHEMA_INBID	120-138	289-314	PHEMA_NDVB	93-110
PV/QLY_LASBQ	426-441	PHEMA_INBLE	123-139	302-317	PHEMA_NDWD	93-110
PV/QLY_LASSJ	427-442	PHEMA_INBMD	113-128	282-307	PHEMA_NDVF	93-110
PV/QLY_MOPEI	426-440	PHEMA_INBME	116-132	286-311	PHEMA_NDVM	93-110
PV/M3_RECVD	521-536	PHEMA_INBNA	108-124	288-303	PHEMA_NDVQ	93-110
PV/M3A_HPRQS	380-385	PHEMA_INBOR	123-138	301-316	PHEMA_NDVQ	93-110
PV/M3A_WH/PV8	187-202	PHEMA_INBSI	123-138	301-316	PHEMA_NDVU	93-110
PV/M3A_WH/V1	378-393	PHEMA_INBSJ	116-135	286-313	PHEMA_PHODY	38-53
PV/M3A_WH/V59	383-398	PHEMA_INBJS	116-132	286-309	PHEMA_P11HW	486-503
PV/M3A_WH/V7	383-398	PHEMA_INBVI	116-132	286-311	PHEMA_P13B	111-128
PV/M3A_WH/V8	383-398	PHEMA_INBVK	123-139	303-318	PHEMA_P13H4	111-128
PV/M3A_WH/V8I	383-398	PHEMA_INBVK	108-124	286-301	PHEMA_P13HA	111-128
PV/M3A_WH/VW6	234-249	PHEMA_MUMPM	133-148		PHEMA_P13HT	111-128
PV/M72_IANN	26-40	PHEMA_MUMPR	133-148		PHEMA_P13HU	111-128
PV/M72_IABAN	26-40	PHEMA_MUMPS	133-148		PHEMA_P13HV	111-128
PV/M72_IAFOW	26-40	PHEMA_P11HW	345-380		PHEMA_P13HW	111-128
PV/M72_IAPFR	26-40	PHEMA_P12H	85-81		PHEMA_P13HX	111-128
PV/M72_IAPPW	26-40	PHEMA_P12HT	85-81		PHEMA_P14HA	50-67

PVMT2_JALE1	26-40	PHEMA_P138	324-340		PHEMA_SV41	86-102
PVMT2_JALE2	25-40	PHEMA_P134	324-340		PHEMA_SV5	84-101
PVMT2_JAMAN	26-40	PHEMA_P134	324-340		PHEMA_SV5CM	84-101
PVMT2_JAPUE	25-40	PHEMA_P134T	324-340		PHEMA_SV5CP	84-101
PVMT2_JASIN	25-40	PHEMA_P134U	324-340		PHEMA_SV6LN	84-101
PVMT2_JAUDO	25-40	PHEMA_P134V	324-340		PVF05_VACCC	280-287
PVMT2_JAWIL	25-40	PHEMA_P134V	324-340		PVF06_VACCP	280-287
PVMT2_MYXVL	226-241	PHEMA_P134X	324-340		PVF06_VACCV	281-298
		PHEMA_RINDK	366-383		PVF09_VACCC	176-193
		PHEMA_SV6	7-94		PVF09_VACCV	176-193
		PHEMA_SV6CM	7-94		PVG27_HSV/SA	209-226
		PHEMA_SV6CP	7-94		PVG28_HSV1	173-190
		PHEMA_SV6LN	7-94		PVG38_HSV1	646-666
		PVENV_DHV11	42-57		PVG43_HSV1	621-638
		PVENV_EAV	26-41		PVG87_HSV1	171-188
		PVFP2_FOWPV	88-104		PVG12_HSV1	1252-1269
		PVFP7_CAPIK	89-104		PVG13_HSV4	3073-3080
		PVFUS_VACC6	72-87		PVG12_IBVB	1094-1111
		PVG01_HSVEB	166-184		PVG13B_HSVE1	738-753
		PVG01_HSVII	209-225	3117-332	PVG13B_HSVE4	675-692
		PVG08_HSVII	134-148		PVG13B_HSVEA	736-753
		PVG10_HSVSA	108-124		PVG13B_HSVEB	736-753
		PVG11_HSVII	103-119		PVG13B_HSVEL	736-753
		PVG12_HSVII	270-288		PVG13B_LT/TV6	597-614
		PVG11_SPV1R	76-92		PVG13B_LT/TV8	607-624
		PVG28_HSVII	20-35		PVG13B_LT/TV7	607-624
		PVG36_BPOX2	22-37		PVG13C_PRVIF	180-197
		PVG36_HSVSA	108-123		PVG13E_VZVD	469-486
		PVG37_HSVII	284-289		PVG13F_SV6	401-418
		PVG41_HSVII	244-260		PVG13H_HCMVA	395-382
		PVG46_HSVII	1244-1260		PVG13H_HCMVT	394-381
		PVG55_HSVII	22-37	143-168	PVG14_HSV11	245-262
		PVG56_HSVII	268-283		PVG14_HSV1E	245-262
		PVG58_HSVII	101-117		PVG14I_HSV11	43-60
		PVG58_HSVSA	130-146	330-346	PVG14M_BUNL7	81-98
		PVG59_HSVII	287-282		PVG14M_BUNSH	81-98
		PVG66_HSVII	362-378	516-533	PVG14M_PUJMH	712-729
		PVG71_HSVSA	89-105		PVG14M_PUUMS	712-729
		PVG9_BPPH2	234-249		PVG14M_RVFRV	344-361
		PVG9_BFPZA	234-249		PVG14M_RVFVZ	344-361
		PVG9_SPV1R	67-72		PVGLY_LASSQ	12-94
		PVGF1_IBVB	2210-2226		PVGLY_LASSJ	12-94
		PVGL2_CVBF	123-139	174-190	PVGLY_LYCV	12-94
		PVGL2_CVBL9	123-139	174-190	PVGLY_LYCVW	12-94
		PVGL2_CVBLY	123-139	174-190	PVGLY_MOPEI	12-94
		PVGL2_CVBM	123-138	174-190	PVMI_KEOVD	280-297
		PVGL2_CVBU	31-47	123-139	PVMI_KEOVL	280-297

PVGL2_CVBY	123-139	174-180	264-279		PVMAT_CDVO	148-166
PVGL2_CVM4	95-111	1287-1283			PVMP_MEASI	87-104
PVGL2_CVM6	95-111	1216-1231			PVMP_CAMVC	147-164
PVGL2_CVMJH	95-111	1126-1142			PVMP_CAMVD	147-164
PVGL2_CVPS	442-467	800-816	1274-1280		PVMP_CAMVE	147-164
PVGL2_CVPU	440-465	604-618	793-814	1272-1288	PVMP_CAMVN	147-164
PVGL2_CVPR8	219-233	579-592	1050-1066		PVMP_CAMVS	147-164
PVGL2_CVPRM	218-233	578-592	1050-1068		PVMP_CAMVW	147-164
PVGL2_FIPV	803-819	1277-1293			PVMSA_HPBVO	11-94
PVGL2_IBV6	1058-1071				PVMSA_HPBV2	185-202
PVGL2_IBVB	1058-1070				PVMSA_HPBV4	185-202
PVGL2_IBVD2	1058-1071				PVMSA_HPBVA	174-191
PVGL2_IBVK	1058-1070				PVMSA_HPBVO	11-94
PVGL2_IBVM	1055-1070				PVMSA_HPBVJ	174-191
PVGLB_HSVSA	701-718				PVMSA_HPBVL	174-191
PVGLB_PRVIF	203-218				PVMSA_HPBVN	11-94
PVGLB_VZVD	522-538				PVMSA_HPBVO	174-191
PVGLC_HSVBC	475-480				PVMSA_HPBVP	185-202
PVGLC_HSVE4	444-469				PVMSA_HPBVR	185-202
PVGLC_HSVEB	427-442				PVMSA_HPBVS	11-94
PVGLC_PRVIF	448-461				PVMSA_HPBVN	174-191
PVGLC_VZVD	150-188				PVMSA_HPBVY	174-191
PVGLC_VZVS	150-168				PVMSA_HPBVZ	174-191
PVGLD_HSV11	78-94				PVMT2_IANN	25-42
PVGLD_HSV2	79-84				PVMT2_IABAN	25-42
PVGLE_PRVRI	3-84				PVMT2_IAFOW	25-42
PVGLF_BRSA	205-221	285-280			PVMT2_IAPR	25-42
PVGLF_BRSC	205-221	285-280			PVMT2_IAPFW	25-42
PVGLF_BRSR	205-221	285-280			PVMT2_IALE1	25-42
PVGLF_CDVO	389-414				PVMT2_IALE2	25-42
PVGLF_HRSV1	205-221	285-280			PVMT2_IAMAN	25-42
PVGLF_HRSV4	205-221	285-280			PVMT2_IARUE	25-42
PVGLF_HRSV1	205-221	285-280			PVMT2_IASIN	25-42
PVGLF_HRSV1	205-221	285-280			PVMT2_IAUDIO	25-42
PVGLF_MEASE	286-302				PVMT2_IAWIL	25-42
PVGLF_MEAS1	288-305					
PVGLF_MEASY	286-302					
PVGLF_MUMPM	276-282					
PVGLF_MUMPR	276-282					
PVGLF_MUMPS	6-94	276-282				
PVGLF_NDVA	273-288					
PVGLF_NDVB	273-288					
PVGLF_NDVA	273-288					
PVGLF_NDVT	273-288					
PVGLF_NDVTG	273-288					
PVGLF_NOVJ	273-288					
PVGLF_PHODV	269-285	367-383				

PVGFL RINDK	282-288
PVGFL RINDL	282-288
PVGFL TRIV	175-191
PVGLI VZVD	278-283
PVGLM HANTB	365-371
PVGLM HANTH	489-515
PVGLM HANTL	489-515
PVGLM HANTV	489-515
PVGLM PTPV	743-758
PVGLM PUUMH	608-626
PVGLP PUUMS	605-625
PVGLY LAS59	12-94
PVGLY SEOUR	365-371
PVGLY SEOUS	365-371
PVGLM LIUK	828-842
PVGLP BEV	869-885
PVGLY LAS59	12-94
PVGLY LASUJ	12-94
PVGLY LYCVA	12-94
PVGLY LYCNW	12-84
PVGLY MOPEI	12-84
PVGLY PIARV	12-84
PVGNM CPNV	1021-1037
PVM3 RE01D	621-638
PVMAT MUMPS	18-207
PVMAT NDVA	135-151
PVMAT NDVB	135-151
PVMAT RI2T	189-205
PVMAT SV41	189-205
PVMAT SV5	98-114
PVMP CAMVC	118-134
PVMP CAMVD	118-134
PVMP CAMVE	118-134
PVMP CAMVN	118-134
PVMP CAMVS	118-134
PVMP CAMVW	118-134
PVMP FMVD	116-131
PVMSA_HPBGS	380-395
PVMSA_HPBV8	187-202
PVMSA_WHV1	375-393
PVMSA_WHV59	383-398
PVMSA_WHV7	383-398
PVMSA_WHV8	383-398
PVMSA_WHV81	383-398
PVMSA_WHVv6	234-249
PVMT2_IANIN	26-40
PVMT2_IABAN	25-40
PVMT2_IAFOW	25-40

PVMT2_JAFPR	26-40
PVMT2_JAFPW	26-40
PVMT2_JALE1	26-40
PVMT2_JALE2	26-40
PVMT2_JAMAN	26-40
PVMT2_JAPUE	26-40
PVMT2_JASIN	26-40
PVMT2_JAUDIO	26-40
PVMT2_JAWIL	25-40
PVMT9_MYYVL	226-241

TABLE VII

Search Results Summary for P3CTLZIP, P4CTLZIP,
P5CTLZIP, and P6CTLZIP Motifs

P3CTLZIP	P4CTLZIP	PECTLZIP	PECTLZIP
LIBRARY FILE	LIBRARY FILE	LIBRARY FILE	LIBRARY FILE
PENV_BIV27	PENV1_FRSFV	380-389	PENV1_FRSFV
PENV_CAEVC	PENV_AVISU	98-117	PENV2_FRSFV
PENV_CAEVG	PENV_BIV27	147-166	PENV_BAEVM
PENV_HV2BE	PENV_HV1ZH	123-142	PENV_FIVE
PENV_HV2D1	PENV_HV2D2	8-28	PENV_FIVSD
PENV_HV2S1	PENV_HV2SB	778-787	PENV_FIVT2
PENV_HV2NZ	PENV_JSRV	651-660	PENV_FVLGL
PENV_HV2RO	PENV_RSVP	553-562	PENV_FOAMV
PENV_HV2SB	PHEMA_VACCC	173-182	PENV_FSVGA
PENV_HV2ST	PHEMA_VACCI	173-182	PENV_HV1C4
PENV_JSRV	PHEMA_VACCT	173-182	PENV_HV2CA
PHEMA_P12H	PHEMA_VACCV	173-182	PENV_MLVF5
PHEMA_P12HT	PHEMA_BEV	62-81	PENV_MMVTF
PHEMA_SV41	PENV_MCV1	61-80	PENV_MMVTF6
PENV_THOGV	PENV_MCV2	61-80	PENV_OMVVS
PVG1_B_BPP22	PVFUS_ORFNZ	29-48	PENV_RSVP
PVG2A_BPT4	PVG01_HSEVE	169-188	PENV_SFV1
PVG3B8_HSVSA	PVG01_VACCC	316-386	PENV_SFV3L
PVG3D0_HSV1	PVG01_VACCV	315-334	PENV_SIVM1
PVG3D0_HSVSA	PVG01_VARV	316-386	PENV_SIVMK
PVG3D1_BPT4	PVG08_BPT4	627-848	PENV_SIVML
PVG3D1_HSV1	PVG10_HSV1	36-54	PENV_SIVS4
PVG3D5_HSV1	PVG11_HSV1	103-122	PENV_SIVSP
PVG3F1_IBVB	PVG1_BPPH2	31-50	PHEMA_CDVO
PVG3J2_CVH22	PVG1_SPV1R	689-878	PHEMA_CVBLY
PVG3J2_IBVB	PVG20_BPT4	231-250	PHEMA_CVBM
PVG3J2_IBVB	PVG32_VZVD	90-109	PHEMA_CVBO
PVG3J2_IBVD2	PVG36_BPK3	132-151	PHEMA_CVHOC
PVG3J2_IBVK	PVG37_BPT2	18-38	PHEMA_CVMA5
PVG3J2_IBVM	PVG37_BPT4	18-38	PHEMA_JACKG
PVG3J8_HSVB1	680-678	656-644	PHEMA_JADMA
PVG3J8_HSVBC	692-710	1038-1057	PHEMA_MUMPMV
PVG3J8_HSVSA	654-602	62-81	PHEMA_MUMPR
PVG3J8_LTVC6	PVG43_BPPF3	380-389	PHEMA_SFV1
PVG3J8_LTVC8	PVG48_BPPF1	337-366	PHEMA_SFV2L
PVG3J8_LTVC8	PVG59_HSV1	142-161	PHEMA_SFODV
PVG3J8_LTVC8	PVG61_HSV1	117-138	PHEMA_P1HHW
PVG3LC_V2VD	PVG67_HSV1	318-337	PHEMA_P12H
PVG3LC_V2VS	PVG671_IBVB	1587-1806	PHEMA_P12HT
PVG3LF_P13H4	PVGL2_CVBF	991-1010	PHEMA_RINDL
PVG3LF_HSVBG	PVGL2_CVBL9	991-1010	PHEMA_SEND6
PVG3LF_HSVE4	PVGL2_CVBLY	991-1010	PHEMA_SENDF
PVG3LF_HSVEB	PVGL2_CVBM	991-1010	PHEMA_SENDH
PVG3LI_HSV11	PVGL2_CVBO	991-1010	PHEMA_SENDJ
PVG3M_BPMV	PVGL2_CBVV	991-1010	PHEMA_SENDZ
PVH01_VACCC	PVGL2_CVH22	1115-1134	PENV_LELV

PVM01_VACCV	83-101	126-144	PVGL2_CVM4	898-1018		PVENV_THQV	356-378		HEMA_P12H	13-34
PVM1_1EOVD	227-246		PVGL2_CVMA5	897-898		PVGL01_VACCC	298-318		HEMA_P12HT	13-34
PVM1_1EOVL	227-246		PVGL2_CVMJH	898-897		PVGL01_VACCV	237-267		HEMA_SV6	7-28
PVMAT_HRSVA	44-62		PVGL2_CVPFS	84-83	1038-1067	PVGL01_VARV	298-318		HEMA_SV6CM	7-28
PVMAT_NDVA	190-208		PVGL2_CVPPU	84-83	1036-1055	PVGL08_VACCC	31-51		HEMA_SV6CP	7-28
PVMAT_NDVB	190-208		PVGL2_CVPR8	814-833		PVGL08_VARV	31-51		HEMA_SV6LN	7-28
PVMP_CAMVC	183-201		PVGL2_CVPRM	814-833		PVGL09_BPF1	25-45		PVGL01_HSVB	169-180
PVMP_CAMVD	183-201		PVGL2_FIPV	1041-1080		PVGL12_HSV1	161-171		PVGL01_HSV1	589-610
PVMP_CAMVE	183-201		PVGL2_IBV6	668-607	771-780	PVGL22_HSV1	300-320		PVGL23_HSV1	314-335
PVMP_CAMVE	183-201		PVGL2_IBVB	667-606	770-788	PVGL39_HSV1	648-688	970-990	PVGL37_BPOX2	66-86
PVMP_CAMVN	183-201		PVGL2_IBVD2	668-607	771-780	PVGL61_HSV1	29-49		PVGL43_HSV1	167-178
PVMP_CAMVS	183-201		PVGL2_IBVK	667-606	770-789	PVGL63_HSV1	338-358		PVGL65_HSV1	288-309
PVMP_CAMVW	183-201		PVGL2_IBVM	667-608	770-788	PVGL65_HSV1	117-137		PVGL65_HSVSA	86-106
PVMP_FMVD	180-188		PVGLB_HCMVA	708-725		PVGL74_HSVSA	124-144		PVGL58_HSV1	1155-1176
			PVGLB_HCMVT	707-728		PVGL2_IBV6	328-348		PVGL58_HSVSA	268-287
			PVGLB_HSVBU	117-136		PVGL2_IBVB	327-347		PVGL60_HSV1	30-51
			PVGLB_1LT76	268-275		PVGL2_IBVD2	328-348		PVGL63_HSV1	238-259
			PVGLB_1LTV8	268-285		PVGL2_IBVD3	328-348		PVGL61_IBVB	1886-1877
			PVGLB_1LT7V	268-285		PVGL2_IBVK	327-347		PVGH3_HCMVA	167-178
			PVGLC_HSV11	3-84	467-486	PVGL2_IBVM	327-347	378-398	PVGL2_CVBF	1259-1280
			PVGLC_HSV1K	3-94	467-486	PVGL2_IBVU2	310-330		PVGL2_CVBL9	1258-1280
			PVGLC_HSVBC	475-494		PVGL2_IBV	732-752		PVGL2_CVBLY	1259-1280
			PVGLG_CHAV	436-456		PVGLB_HCMVA	760-770		PVGL2_CVBM	1259-1280
			PVGLG_RABVH	312-391		PVGLB_HCMVT	761-771		PVGL2_CVHQ	1259-1280
			PVGLI_HSE1B	44-63		PVGLB_HSV23	79-89		PVGL2_CBV	1259-1280
			PVGLI_VZD	278-297		PVGLB_HSV2H	79-89		PVGL2_CVCM4	1317-1338
			PVGLM_BUNGE	117-136		PVGLB_HSV28	86-86		PVGL2_CVMA6	1256-1286
			PVGLM_PHV	162-171		PVGLB_HSV8U	72-82		PVGL2_CVMAH	1178-1197
			PVGLM_PTPV	987-1018		PVGLB_HSVB2	278-298		PVGLB_HSV11	83-104
			PVGLM_PUUMH	165-174		PVGLB_HSVSA	83-83		PVGLB_HSVIF	B2-103
			PVGLM_PUUMS	165-174		PVGLB_MCMVS	738-758		PVGLB_HSVIK	B2-103
			PVGLM_RFV	830-849		PVGLE_PI3HA	283-303		PVGLB_HBVP	B3-104
			PVGLM_RFVZ	830-849		PVGLG_RABV	454-474		PVGLB_MCMVS	136-156
			PVGLM_UJK	665-674		PVGLG_RABVH	454-474		PVGLC_PRVIF	448-467
			PVGLY_LYCVW	88-108		PVGLG_RABVP	454-474		PVGLF_CDVO	338-357
			PVGNB_CPMV	1166-1184		PVGLG_RABVS	454-474		PVGLF_MEASE	224-245
			PVM3_1EOVD	621-540		PVGLG_RABVT	454-474		PVGLF_MEASI	227-248
			PVME1_CVBM	171-180		PVGLH_MCMVS	670-690		PVGLF_MEASY	224-245
			PVME1_CVH22	136-165		PVGLM_BUNL7	1326-1346		PVGLF_MUMPM	446-467
			PVME1_CVPFS	174-193		PVGLM_BUNSH	1326-1346		PVGLF_MUMPR	446-467
			PVME1_CVPPU	174-193		PVGLM_BUNYW	986-1018		PVGLF_MUMPS	446-467
			PVME1_CVPRM	174-193		PVGLM_HANTB	989-1018		PVGLF_P10D	305-326
			PVME1_CVTKE	171-180		PVGLM_HANTH	1000-1020		PVGLF_P11HC	468-477
						PVGLM_HANTL	1001-1021		PVGLF_P12H	450-471
						PVGLM_HANTV	1001-1021		PVGLF_P12HG	460-471
						PVGLM_RFVZ	1158-1178		PVGLF_P12HT	450-471
						PVGLM_SEOUR	1000-1020		PVGLF_P13B	405-426

PVGLM SEQUS	999-1010	PVGLF PR3H4	463-474
PVGLM UUK	925-945	PVGLF RINDK	220-241
PVGLY LYCVIA	12-32	PVGLF RINDL	220-241
PVIALY LYCVW	12-32	PVALF SEND5	460-481
PVGLY PIARV	12-32	PVGLF SENDF	460-481
PVGNB CPMV	141-161	PVGLF SENDH	460-481
PVMAT MUMPS	310-330	PVGLF SENDJ	460-481
PVMAT NDVA	309-329	PVGLF SENDZ	460-481
PVMAT NDVB	309-329	PVGLF SV41	463-474
PVMAT PI2HT	308-328	PVGLF SV6	448-467
PVMAT PI4HA	312-332	PVGLH HCMVA	681-712
PVMAT PI4HB	312-332	PVGLH HCMVT	680-711
PVMAT SV41	308-328	PVGLH HSVE4	304-325
PVMAT SV5	308-328	PVGLH HSVEB	287-318
PVME1 IBV6	74-94	PVGLH HSVA	658-679
PVME1 IBVB	74-94	PVGLI HS2	2-23
PVME1 IBVB2	74-94	PVGLI HV23	2-23
PVME1 IBVK	74-94	PVGLM BUNGE	187-218
PVMSA HPBDB	201-221	PVGLM BUNL7	180-211
PVMSA HPBGS	209-229	PVGLM BUNSH	180-211
PVMSA HPBHE	283-313	PVGLM BUNWV	183-214
PVMSA WHV1	207-227	PVGLY LABSG	237-258
PVMSA WHV59	212-232	PVGLY LASJ	238-259
PVMSA WHV7	212-232	PVGPB EEP	67-88
PVMSA WHV8	212-232	PVM01 VACCC	281-302
PVMSA WHV8I	212-232	PVM01 VACCV	230-251
PVMSA WHVW6	63-83	PVMAT HRSVA	199-160
		PVMAT RINDK	200-221
		PVMAT TRTV	122-143
		PVME1 CYHOC	94-95
		PVMSA HPBDB	201-222
		PVMSA HPBIV0	70-81
		PVMSA HPBV2	244-265
		PVMSA HPBV4	244-265
		PVMSA HPBV9	244-265
		PVMSA HPBVIA	233-254
		PVMSA HPBVD	70-81
		PVMSA HPBVI	233-254
		PVMSA HPBVJ	233-254
		PVMSA HPBVL	233-254
		PVMSA HPBVN	70-91
		PVMSA HPBVO	233-254
		PVMSA HPBVP	244-285
		PVMSA HPBVR	244-285
		PVMSA HPBVS	70-91
		PVMSA HPBVW	233-254
		PVMSA HPBVY	233-254

PV/MSA_HPBVZ	233-254
PV/MT2_JAANN	25-46
PV/MT2_JABAN	25-46
PV/MT2_JAFOW	25-46
PV/MT2_JAFPR	25-46
PV/MT2_JAFFW	25-46
PV/MT2_JALE1	25-46
PV/MT2_JALE2	25-46
PV/MT2_JAMAN	25-46
PV/MT2_JAPUE	25-46
PV/MT2_JASIN	25-46
PV/MT2_JAUJO	25-46
PV/MT2_JAWIL	25-46

TABLE VIII

Search Results Summary for P7CTLZIP,
P8CTLZIP, and P9CTLZIP Motifs

P7CTLZIP		P8CTLZIP		P9CTLZIP		
LIBRARY FILE		LIBRARY FILE		LIBRARY FILE		
PENV_BAEVM	202-224.	PENV1_FRSFV	380-403	PENV_BLVAF	303-327	
PENV_HV1B1	49B-520	PENV2_FRSFV	380-403	PENV_BLVAU	303-327	
PENV_HV1B8	493-516	PENV_BV06	178-201	PENV_BLVAV	303-327	
PENV_HV1BN	494-516	PENV_BV27	207-230	PENV_BLVB2	303-327	
PENV_HV1BR	503-526	PENV_FOAMV	864-887	PENV_BLB6	303-327	
PENV_HV1EL	495-617	PENV_HV123	176-198	PENV_BLVJ	303-327	
PENV_HV1H2	498-620	PENV_HV2BE	3-28	PENV_FVPE	781-805	
PENV_HV1H3	498-620	PENV_HV2CA	760-773	PENV_FVSD	778-803	
PENV_HV1J3	610-632	PENV_HV2D1	3-26	772-796	PENV_FV72	
PENV_HV1JR	490-512	PENV_HV2G1	772-795	780-804		
PENV_HV1KB	604-528	PENV_HV2N2	777-800	PHEMA_CVBLY	391-415	
PENV_HV1MA	600-522	PENV_JSRV	541-564	PHEMA_CVBM	391-415	
PENV_HV1MF	498-518	PENV_SV1	864-887	PHEMA_CVHOC	391-415	
PENV_HV1ND	488-510	PENV_SV3L	861-884	PHEMA_INCCA	442-466	
PENV_HV1PV	498-520	PENV_SV1M1	803-828	PHEMA_INCEN	430-454	
PENV_HV1S1	488-511	PENV_SV1MK	802-825	PHEMA_INCGL	430-454	
PENV_HV1Z2	123-146	486-517	PENV_SV1ML	801-824	PHEMA_INCHY	429-453
PENV_HV1Z6	497-519	PENV_SV1S4	806-828	PHEMA_INCJH	443-487	
PENV_HV1Z8	506-627	PENV_SV1SP	810-833	PHEMA_INCKY	429-453	
PENV_HV1ZH	498-620	PHEMA_CDVO	200-223	PHEMA_INCMI	429-453	
PENV_JSRV	376-398	PHEMA_P12H	65-98	PHEMA_INCNA	429-453	
PENV_MPMV	213-236	PHEMA_P12HT	65-88	PHEMA_INCP1	430-454	
PENV_SRV1	213-236	PVF11_VACCC	161-184	PHEMA_INCP2	430-454	
PHEMA_IAC	37-59	PVF15_VACCC	25-48	PHEMA_INCP3	430-454	
PHEMA_IABAN	21-43	PVF15_VACCP	3-28	PHEMA_INCTA	430-454	
PHEMA_IADA3	37-59	PVG1L_AMEPV	313-336	PHEMA_INCYA	430-454	
PHEMA_IADH2	21-43	PVG2B_HSV1	491-514	PHEMA_MUMPM	101-126	
PHEMA_IADH3	21-43	PVG43_HSV1	322-345	PHEMA_MUMPR	101-126	
PHEMA_IADH4	21-43	PVG52_HSV1	229-252	PHEMA_MUMPS	101-126	
PHEMA_IADH5	21-43	PVG67_HSV1	722-745	PHEMA_P1HHW	28-53	
PHEMA_IADH6	21-43	PVG12_CVBF	10-33	PENV_BEV	62-86	
PHEMA_IADH7	21-43	PVG12_CVBL8	651-674	PVF05_VACCC	280-304	
PHEMA_IADM2	37-59	PVG12_CVBLY	10-33	PVF05_VACCP	280-304	
PHEMA_IADM4	28-60	PVG12_CVMA4	1267-1280	PVF05_VACCV	281-305	
PHEMA_IADU3	37-59	PVG12_CVMA6	1215-1238	PVF08_VACCC	178-200	
PHEMA_IAEW8	21-43	PVG12_CVM/H	1126-1149	PVF09_VACCV	178-200	
PHEMA_IAEW7	37-59	PVG12_CVPPS	1274-1287	PVG01_VZVD	68-82	
PHEMA_IAMAO	37-59	PVG12_CVPPU	1272-1285	PVG10_HSVSA	356-379	
PHEMA_IAME1	37-59	PVG12_CVPR8	1050-1073	PVG12_HSVSA	68-82	
PHEMA_IAME2	37-59	PVG12_CVFRM	1050-1073	PVG19_HSVI	88-112	
PHEMA_IAME6	21-43	PVG12_FIPV	1277-1300	PVG28_HSVI	173-197	
PHEMA_IANT6	37-59	PVG12_BV6	196-219	PVG43_HSVI	108-133	
PHEMA_IAUQ7	21-43	PVG12_BVB	195-218	PVG67_HSVI	108-132	
PHEMA_IATKM	33-56	PVG12_BVD2	198-219	PVG72_HSVI	720-744	
PHEMA_IAUDIO	37-59	PVG12_BVD3	198-219	PVGf1_BVB	3601-3625	

PHEMA JAV17	38-80	PVGL2 IBVK	195-218	PVGLB HSVMD	688-613
PHEMA JAX31	37-59	PVGL2 IBVM	195-218	PVGLB ILTV6	597-821
PHEMA JAZCO	37-59	PVGL2 IBVU1	178-201	PVGLB ILTV8	607-831
PHEMA JAZH2	21-43	PVGL2 IBVU2	178-201	PVGLB ILTV7	607-831
PHEMA JAZH3	21-43	PVGL2 IBVU3	178-201	PVGL HSV11	413-437
PHEMA JAZUK	37-58	PVGLB HCMVA	535-568	PVGL E2VID	469-493
PHEMA PHODV	38-58	PVGLB HCMVT	536-559	PVGLF SV6	401-426
PHEMA P12H	65-87	PVGLB HSV5A	433-506	PVGLH HCMVA	674-598
PHEMA P12HT	65-87	PVGLB MCMVS	606-689	PVGLH HCMVT	673-597
PVFPT CAPVK	88-111	PVGLC HSV11	467-480	PVGLH HSV11	443-487
PVFUS VACCB	72-84	PVGLC HSV1K	467-480	PVGLH HSV1E	443-487
PVG01 HSV1	317-339	PVGLC HS2	435-458	PVGLM BUNL7	31-55
PVG03 VACCC	60-72	PVGLC HSV23	438-458	PVGLM BUNSH	31-55
PVG03 VARV	60-72	PVGLM BUNL7	1387-1410	PVGLM HANTH	694-718
PVG04 VACCC	11-33	PVGLM BUNSH	1387-1410	PVGLM RVEV	344-368
PVG04 VARV	11-33	PVGLM UK	906-989	PVGLM RVEVZ	344-368
PVG10 HSV1	88-110	PVGLY JUNIN	12-35	PVGLM UUK	661-586
PVG28 HSV11	173-196	PVGLY LAS6A	12-35	PVGNM CPMV	311-336
PVG28 HSV11	20-42	PVGLY LAS6J	12-35	PVGL2 EBV	657-681
PVG46 HSV11	134-168	PVGLY LYCVA	12-35	PVGL3 EBV	654-878
PVG48 HSVSA	71-83	PVGLY LYCWN	12-35	PVM1 REOVD	280-304
PVG58 HSVSA	268-288	PVGLY MOPEI	12-35	PVM1 REOVL	280-304
PVG59 HSV1	267-288	PVGLY TACV	12-35	PVM21 REOVD	168-192
PVG5 SPV4	42-84	PVGLY TACV6	12-35	PVM22 REOVD	168-192
PVG60 HSV1	63-75	PVGLY TACV7	12-35	PVM2 REOJV	168-192
PVG65 HSV1	1347-1369	PVGLY TACVT	12-35	PVM2 REOVL	168-192
PVG8 SPV1R	60-82	PVGNM_CPMV	741-784	PVMAT MEASI	87-111
PVGL2 IBV6	1056-1078	PVM1 REOVD	324-347	PVMAT SSPV6	314-338
PVGL2 IBV6	1056-1077	PVM1 REOVL	454-477	PVM1 CVBM	137-161
PVGL2 IBVD2	1056-1078	PVMAT NUMPS	227-250	PVM1 CVHOC	137-161
PVGL2 IBVK	1056-1077	PVMSA HBDB	288-292	PVM1 CVTK6	137-161
PVGL2 IBV	1056-1077	PVMSA HBDC	268-291	PVM1 IBV6	74-88
PVGLB HSV8U	117-139	PVMSA HBDDU	231-254	PVM1 IBV8	74-88
PVGLB HSVB2	745-767	PVMSA HBBDW	269-292	PVM1 IBVB2	74-88
PVGLC HSVMB	398-421	PVMSA HBBE	238-259	PVM1 IBVK	74-88
PVGLC HSVMG	398-420			PVMSA HPBGS	271-285
PVGLC HSVMM	398-421			PVMSA WHV1	289-283
PVGLF BREVA	266-287	482-604		PVMSA WHV58	274-288
PVGLF BREVC	484-608			PVMSA WHV7	274-288
PVGLF BR5VR	484-608			PVMSA WHV8	274-288
PVGLF HRSV1	484-608			PVMSA WHV81	274-288
PVGLF HRSV4	484-608			PVMSA WHVW6	126-149
PVGLF HRSV1	484-608				
PVGLF HRSV1	484-608				
PVGLF TRTV	462-474				
PVGLG IHNV	77-89				
PVGLG VHSV0	406-428				

PVGLH HSVE4	814-836
PVGLH HSVEB	807-829
PVGLI HCMVA	168-180
PVGLM PTPV	743-765
PVGLP BEV	430-452
PVGLY LASSG	426-448
PVGLY LASSJ	427-449
PVGLY MOREI	425-447
PVGP2 EBV	667-678
PVGP3 EBV	854-878
PVM1 REOVD	414-438
PVM1 REOVL	414-438
PVM3 REOVD	304-326
PVMAT PIHHC	185-217
PVMAT PI2HT	132-154
PVMAT SENDF	185-217
PVMAT SENDH	186-217
PVMAT SENDZ	185-217
PVMAT SV41	132-154
PVMEB EBV	131-153
PVMP CERV	283-315

TABLE IX

Search Results Summary for P12CTLZIP Motif

PENV_HV12H	123-142	438-463	498-520
PENV_HV28E	3-26	750-776	781-804
PENV_HV2CA	760-777		
PENV_HV2D1	3-28	741-768	772-786
PENV_HV2D2	9-28		
PENV_HV2G1	741-768	772-795	
PENV_HV2N2	742-767	777-800	
PENV_HV2R0	751-778		
PENV_HV2SB	743-768	778-804	
PENV_HV2ST	745-770		
PENV_JSRV	104-119	298-325	378-398
PENV_MCF1	600-821		
PENV_MCF3	601-822		
PENV_MLVAV	630-661		
PENV_MLVCB	626-646		
PENV_MLVFS	638-660		
PENV_MLVFF	639-660		
PENV_MLVFP	639-660		
PENV_MLVHO	626-647		
PENV_MLVKI	187-188		
PENV_MLVMO	628-650		
PENV_MLVRD	624-645		
PENV_MLVRK	624-645		
PENV_MMTVB	643-663		
PENV_MMTVG	643-663		
PENV_MPMV	213-236		
PENV_MSVFB	170-191		
PENV_OMVVS	75-100	668-683	
PENV_RMCFV	603-824		
PENV_RSVP	42-89	533-552	
PENV_SFV1	300-325	710-727	864-887
PENV_SFV3L	167-178	304-328	707-724
PENV_SIVVA1	437-458		
PENV_SIVAG	442-463		
PENV_SIVAI	421-442		
PENV_SIVAT	435-458		
PENV_SIVGB	93-109		
PENV_BIVM1	769-783	803-826	
PENV_BIVM2	139-154	796-792	802-826
PENV_SIVMK	138-154	784-791	801-824
PENV_SIVML	769-789	806-829	
PENV_SIVS4	773-793	810-833	
PENV_SMSAV	42-63		
PENV_SRV1	213-235		
PHEMA_CDVO	36-53	200-223	
PHEMA_CVBLY	391-416		
PHEMA_CVBM	391-415		

PHEMA_CVBQ	391-415
PHEMA_CVHOC	381-415
PHEMA_CVMA6	402-423
PHEMA_CVMS	403-418
PHEMA_IAAIC	37-59
PHEMA_IABAN	21-43
PHEMA_IABUD	320-337
PHEMA_IACKA	320-337
PHEMA_IACKG	81-101
PHEMA_IACKP	302-319
PHEMA_IACKQ	302-319
PHEMA_IACKS	319-338
PHEMA_IACKV	230-248
PHEMA_IADA1	320-337
PHEMA_IADA2	319-336
PHEMA_IADA3	37-59
PHEMA_IADC2	320-337
PHEMA_IADE1	288-287
PHEMA_IADH1	308-323
PHEMA_IADH2	21-43
PHEMA_IADH3	21-43
PHEMA_IADH4	21-43
PHEMA_IADH6	21-43
PHEMA_IADH8	21-43
PHEMA_IADH7	21-43
PHEMA_IADM2	37-59
PHEMA_IADM4	28-50
PHEMA_IADN2	320-337
PHEMA_IADU3	37-59
PHEMA_IAE8	21-43
PHEMA_IEN7	37-59
PHEMA_IAPR	230-246
PHEMA_IAGRE	320-337
PHEMA_IAGU2	320-337
PHEMA_IAGUA	319-338
PHEMA_IAHAL	221-338
PHEMA_IAHAR	230-246
PHEMA_IAHCB	230-246
PHEMA_IAHC7	230-246
PHEMA_IAHCD	230-246
PHEMA_IAHDE	230-246
PHEMA_IAHFO	236-252
PHEMA_IAHK6	321-338
PHEMA_IAHK7	238-252
PHEMA_IAHLE	230-246
PHEMA_IAHLO	230-246
PHEMA_IAHMI	238-252

PHEMA IAHRIM	238-252	321-338
PHEMA IAHRIN	316-332	
PHEMA IAHP	316-332	
PHEMA IAHRQ	238-252	321-338
PHEMA IAHS	238-252	321-338
PHEMA IAHSF	230-248	316-332
PHEMA IAHSW	230-248	316-332
PHEMA IAHTE	238-252	321-338
PHEMA IAHTO	238-252	321-338
PHEMA IAHUR	238-252	321-338
PHEMA IAJAP	317-334	
PHEMA IAMAA	187-223	318-338
PHEMA IAMAB	202-228	324-341
PHEMA IAMAO	31-69	322-339
PHEMA IAME1	37-59	322-339
PHEMA IAME2	37-59	322-339
PHEMA IAME8	21-43	
PHEMA IAMIN	85-101	231-247
PHEMA IANT6	37-59	322-339
PHEMA IAPIL	320-337	
PHEMA IAQU7	21-43	306-323
PHEMA IAQUD	320-337	
PHEMA IAQZ2	320-337	
PHEMA IAQZ2	321-338	
PHEMA IAQZ4	230-246	316-332
PHEMA IAQZ5	33-66	320-337
PHEMA IAQZI	233-249	
PHEMA IAQZR	230-248	
PHEMA IAQZW	229-246,	
PHEMA IAQZO	37-59	322-339
PHEMA IAQZV	38-60	323-340
PHEMA IAQZI	37-59	
PHEMA IAQZO	37-59	322-339
PHEMA IAQZH2	21-43	308-323
PHEMA IAZH3	21-43	308-323
PHEMA IAZUK	37-59	322-339
PHEMA INBAA	116-131	286-310
PHEMA INBBE	123-139	303-318
PHEMA INBBO	116-132	283-308
PHEMA INBEN	123-139	301-316
PHEMA INBFU	108-124	286-301
PHEMA INBGL	119-135	288-311
PHEMA INBHK	119-132	283-308
PHEMA INBIB	108-124	288-303
PHEMA INBID	120-136	288-314
PHEMA INBLE	123-139	302-317
PHEMA INBMD	113-128	282-307

PHEMA_INBME	116-132	298-311
PHEMA_INBNA	108-124	288-303
PHEMA_INBOR	123-139	301-316
PHEMA_INBSI	123-139	301-316
PHEMA_INBSJ	118-135	298-313
PHEMA_INBUS	116-132	294-309
PHEMA_INBVI	116-132	298-311
PHEMA_INBVK	123-139	303-318
PHEMA_INBYB	108-124	298-301
PHEMA_INCCA	442-466	
PHEMA_INCEM	430-454	
PHEMA_INCAL	430-454	
PHEMA_INCHY	428-453	
PHEMA_INCJH	443-467	
PHEMA_INCKY	428-453	
PHEMA_INCMI	429-453	
PHEMA_INCNA	428-453	
PHEMA_INCP1	430-454	
PHEMA_INCP2	430-454	
PHEMA_INCP3	430-454	
PHEMA_INCTA	430-454	
PHEMA_INCYA	430-454	
PHEMA_MUMPM	133-148	225-246
PHEMA_NUMPR	101-126	133-148
PHEMA_MUMPS	101-126	133-148
PHEMA_NDVA	93-110	
PHEMA_NDVB	93-110	
PHEMA_NDVD	93-110	
PHEMA_NDVH	93-110	
PHEMA_NDVI	93-110	
PHEMA_NDVM	93-110	
PHEMA_NDVQ	93-110	
PHEMA_NDVTG	93-110	
PHEMA_NDVTU	93-110	
PHEMA_PHODV	38-58	213-234
PHEMA_P11HW	28-53	322-342
PHEMA_P12H	13-40	05-88
PHEMA_P12HT	13-40	66-88
PHEMA_P13B	111-128	272-289
PHEMA_P13H4	111-128	272-289
PHEMA_P13HA	111-128	272-289
PHEMA_P13HT	111-128	272-289
PHEMA_P13HU	111-128	272-289
PHEMA_P13IV	111-128	272-288
PHEMA_P13IW	111-128	272-288
PHEMA_P13HX	111-128	272-288
PHEMA_P14HA	50-67	

PHEMA_RINDK	368-383
PHEMA_RINDL	4-30
PHEMA_SEND5	322-342
PHEMA_SEND5F	322-342
PHEMA_SENDH	322-342
PHEMA_SENDJ	322-342
PHEMA_SENDZ	322-342
PHEMA_SV41	65-73
PHEMA_SV5	7-28
PHEMA_SV5CM	7-28
PHEMA_SV5CP	7-28
PHEMA_SV5LN	7-28
PHEMA_VACCC	173-182
PHEMA_VACCI	173-182
PHEMA_VACCT	173-182
PHEMA_VACCV	173-182
PVENV_BEV	62-86
PVENV_DHV11	42-57
PVENV_EAV	26-41
PVENV_LELV	27-47
PVENV_MCV1	61-80
PVENV_MCV2	61-80
PVENV_THROAV	196-221
PVF05_VACCC	280-305
PVF05_VACCP	280-305
PVF05_VACCV	280-305
PVF09_VACCC	176-200
PVF09_VACCV	176-200
PVF11_VACCC	161-184
PVF15_VACCC	25-48
PVF15_VACCP	3-28
PVF1 FOWPV	287-323
PVF2 FOWPV	68-104
PVF7 CAPVK	88-111
PVF7 FOWPV	65-80
PVF8 CAPVK	51-78
PVF8_ORENZ	28-48
PVF16_VACCC8	72-94
PVG01_HSVEB	169-196
PVG01_HSVI1	210-225
PVG01_VACCC	298-318
PVG01_VACCV	237-267
PVG01_VARV	298-318
PVG01_VZVD	68-82
PVG03_VACCC	60-72
PVG03_VARV	60-72
PVG04_VACCC	11-33

PVG04 VARV	11-33
PVG08 VACCC	31-51
PVG08 VARV	31-51
PVG08 HSV11	134-148
PVG10 HSV11	169-185
PVG10 HSV11	35-54
PVG10 HSVSA	108-124
PVG11 HSV11	355-378
PVG11 HSV11	103-122
PVG12 HSV11	160-178
PVG12 HSV11	151-178
PVG12 HSVSA	270-288
PVG16 HSVEB	88-92
PVG19 HSV11	184-209
PVG19 HSV11	88-112
PVG1L AMEPV	313-336
PVG1 L SPVIR	78-92
PVG22 HSV11	659-678
PVG23 HSV11	300-327
PVG27 HSV11	314-335
PVG27 HSV11	168-184
PVG27 HSVSA	208-228
PVG28 HSV11	173-187
PVG28 HSVSA	491-518
PVG29 HSV11	14-40
PVG29 HSV11	20-42
PVG30 HSV11	166-181
PVG32 VZVD	80-108
PVG36 HSVSA	108-123
PVG37 HSV11	344-362
PVG37 HSV11	284-299
PVG39 HSV11	970-980
PVG40 HSV11	648-675
PVG41 HSV11	14-32
PVG41 HSV11	11-38
PVG43 HSV11	62-81
PVG43 HSV11	109-133
PVG46 HSV11	167-178
PVG48 HSV11	134-169
PVG48 HSV11	680-607
PVG48 HSVSA	937-983
PVG49 HSV11	1244-1270
PVG50 HSV11	71-83
PVG50 HSV11	6-30
PVG50 HSVSA	68-83
PVG50 HSVSA	63-81
PVG51 HSV11	95-117
PVG51 HSV11	208-233
PVG52 HSV11	28-49
PVG52 HSV11	84-102
PVG52 HSV11	229-252
PVG55 HSV11	22-37
PVG55 HSV11	143-158
PVG55 HSVSA	288-309
PVG55 HSV11	86-106
PVG55 HSV11	1165-1176
PVG58 HSV6A	130-146
PVG58 HSV6A	286-288
PVG58 HSV11	283-318
PVG58 HSV11	142-161
PVG58 HSV11	267-289
PVG5 SPV4	30-51
PVG5 SPV4	42-64
PVG60 HSV11	63-76
PVG61 HSV11	78-102
PVG61 HSV11	117-138
PVG63 HSV11	238-259
PVG64 HSV11	336-363
PVG64 HSV11	420-445
PVG65 HSV11	117-137
PVG65 HSV11	185-173
PVG67 HSV11	362-378
PVG67 HSV11	618-533
PVG67 HSV11	1147-1174
PVG67 HSV11	1347-1369
PVG67 HSV11	722-745
PVG67 HSV11	1005-1028
PVG67 HSV11	1072-1091
PVG68 SPVIR	318-344
PVG68 SPVIR	60-82

PVGIF_NDVU	273-289			
PVGIF_PHODV	269-285	305-326	367-383	531-558
PVGIF_PI1HC	466-477			
PVGIF_PI2H	460-471			
PVGIF_PI2IG	460-471			
PVGIF_PI2HT	450-471			
PVGIF_PI3B	283-310	405-426	463-474	
PVGIF_PI3I4	2-20	283-310	453-474	
PVGIF_RINDK	220-241	282-298	447-473	
PVGIF_RINDL	220-241	282-298	447-473	
PVGIF_SEND6	460-481			
PVGIF_SENDF	460-481			
PVGIF_SENDH	460-481			
PVGIF_SENDJ	460-481			
PVGIF_SENDZ	460-481			
PVGIF_SV41	463-474			
PVGIF_SV6	401-426	446-467		
PVGIF_TRTV	176-191	462-474		
PVGIG_IHNV	77-89			
PVGIG_RAEEV	464-474			
PVGIG_RAENVH	372-391	454-474		
PVGIL_RAENVP	454-474			
PVGIG_RAENVS	454-474			
PVGIG_RAENVT	454-474			
PVGIL_VHSVIO	406-428			
PVGIL_HCMVA	211-237	365-382	574-598	691-712
PVGIL_HCMVIT	210-238	364-381	573-597	690-711
PVGIL_HSV11	246-262	443-467	803-827	
PVGIL_HSV1E	246-262	443-467	803-827	
PVGIL_HSV6G	314-332			
PVGIL_HSV64	304-326	814-839		
PVGIL_HSV6B	297-318	807-832		
PVGIL_HSVSA	464-479	868-879		
PVGIL_MCMVS	670-690			
PVGIL_HCMVA	168-180			
PVGIL_HSV11	43-60			
PVGIL_HSV6B	44-63			
PVGIL_VZVD	278-297			
PVGIM_BUNGE	117-136	197-222		
PVGIM_BUNL7	31-56	81-98	180-211	1325-1346
PVGIM_BUNSH	31-56	81-98	180-211	1325-1346
PVGIM_BUNYW	183-218	1378-1404		
PVGIM_HANTB	366-371	692-717	800-915	899-1019
PVGIM_HANTH	488-515	694-718	1000-1020	
PVGIM_HANTL	488-515	694-718	1001-1021	
PVGIM_HANTV	488-515	694-718	1001-1021	
PVGIM_PHV	162-171			

PVGIM PTPV	743-765	897-1016	1276-1302
PVGIM PIUUMH	155-174	509-525	712-729
PVGIM PUUMS	185-174	509-525	712-729
PVGIM RVFV	53-80	344-368	830-856
PVGIM RVFVZ	63-80	344-368	830-856
PVGIM SEOUR	355-371	693-718	901-916
PVGIM SEOUS	355-371	692-717	800-916
PVGIM UUK	661-585	655-674	828-842
PVGIP BEV	450-452	898-985	1098-1124
PVGJX PRVRI	149-178		1546-1588
PVGJY JUNIN	12-38	68-108	
PVGJY MOPEI	12-38	425-447	
PVGJY PIARY	12-38	441-466	
PVGJY TACV	12-38		
PVGJY TACV6	12-38		
PVGJY TACV7	12-38		
PVGJY TACV7	12-38		
PVGNB CPMV	141-161	6589-594	757-783
PVGNM BPMV	878-898		
PVGNM CPMV	311-335	741-784	1021-1037
PVGPM EBV	867-681		
PVGPM EBV	854-878		
PVGPM EBV	87-88		
PVM01 VACCC	134-159	177-195	281-302
PVM01 VACCV	83-108	126-144	230-251
PVM1 REOVD	141-168	227-246	280-304
PVM1 REOVL	141-168	227-246	280-304
PVM2 REOVD	168-192		
PVM22 REOVD	168-192		
PVM2 REOVJ	168-182		
PVM2 REOVL	168-192		
PVM3 REOVD	304-328	521-540	
PVMAT BRSVA	37-62		
PVMAT CDVO	148-186	283-309	
PVMAT HRSVA	44-62	139-160	
PVMAT LPMV	311-338		
PVMAT MEASE	283-309		
PVMAT MEASH	283-309		
PVMAT MEASI	67-111		
PVMAT MEASU	283-309		
PVMAT MUMPS	191-207	227-250	310-330
PVMAT NDVA	135-161	190-208	308-328
PVMAT NDVB	135-161	190-208	308-329

PVMAT PI1HC	186-217		
PVMAT PI2HT	132-164	188-205	308-328
PVMAT PI4HA	312-332		
PVMAT PI4HB	312-332		
PVMAT RINDK	200-221	238-280	283-308
PVMAT SENDF	195-217		
PVMAT SENDH	195-217		
PVMAT SENIDZ	195-217		
PVMAT S9PV/B	283-308	314-338	
PVMAT SV41	132-164	188-205	308-328
PVMAT SV5	88-114	132-148	308-336
PVMAT SVCV	141-167		
PVMAT TRTV	122-143		
PVME CVBM	9-38	137-161	171-190
PVME CVH22	138-166		
PVME CVHOC	9-38	84-95	137-161
PVME CVMA6	10-37		
PVME CVMJH	10-37		
PVME CVPFS	174-193		
PVME CVPPU	174-193		
PVME CVPRM	174-193		
PVME CVTKE	9-38	137-161	171-180
PVME IBV6	74-98		
PVME IBVB	74-101		
PVME IBVB2	74-101		
PVME IBVK	74-98		
PVMEM EBV	131-167	178-203	
PVMP CAMVC	118-134	147-164	183-201
PVMP CAMVD	118-134	147-164	183-201
PVMP CAMVE	118-134	147-164	183-201
PVMP CAMVN	118-134	147-164	183-201
PVMP CAMVB	118-134	147-164	183-201
PVMP CAMVV	118-134	147-164	183-201
PVMP CERV	283-318		
PVMP FMVD	115-131	180-198	
PVMP SOCMV	122-147	273-299	
PVMSA HPDBB	201-228	269-295	
PVMSA HPDBC	194-221	268-284	
PVMSA HPDU	167-184	231-267	
PVMSA HPDW	184-221	289-286	
PVMSA HPDGS	208-236	271-296	380-396
PVMSA HPBHE	238-262	293-320	
PVMSA HPBVO	70-98		
PVMSA HPBV2	185-202	244-270	
PVMSA HPBV4	185-202	244-270	
PVMSA HPBV9	244-270		
PVMSA HPBVA	174-181	233-269	

PVMSA	HPBVD	11-28	70-96
PVMSA	HPBVI	233-258	
PVMSA	HPBVJ	174-191	233-259
PVMSA	HPBVJ	174-191	233-259
PVMSA	HPBVN	11-28	70-96
PVMSA	HPBVQ	174-191	233-259
PVMSA	HPBP	186-202	244-270
PVMSA	HPBVR	186-202	244-270
PVMSA	HPBVS	11-28	70-96
PVMSA	HPBVW	174-191	233-259
PVMSA	HPBVY	174-191	233-259
PVMSA	HPBVZ	174-191	233-259
PVMSA	WHV1	207-234	269-293
PVMSA	WHV59	212-239	274-298
PVMSA	WHV77	212-239	274-298
PVMSA	WHV8	212-239	274-298
PVMSA	WHV81	212-239	274-298
PVMSA	WHVv6	125-149	234-249
PVMT2	IAANIN	25-48	
PVMT2	IAJAN	25-48	
PVMT2	IAFOW	25-48	
PVMT2	IAFPR	25-48	
PVMT2	IAFPW	25-48	
PVMT2	IALE1	25-48	
PVMT2	IALE2	25-48	
PVMT2	IAMAN	25-48	
PVMT2	IAPEF	25-48	
PVMT2	IASIN	25-48	
PVMT2	IAUDO	26-48	
PVMT2	IAWIL	26-48	
PVMT9	MYXVL	228-241	

TABLE X

Search Results Summary for P23CTLZIP Motif

P23L2IPC	LIBRARY FILE	98-136
PENV AVISU		
PENV BAEVM	202-240	526-554
PENV BIV06	434-472	555-553
PENV BIV27	554-582	657-688
PENV CAEVQ	44-78	
PENV EIAV1	785-828	
PENV EIAV2	785-828	
PENV EIAV3	785-828	
PENV EIAV5	785-828	
PENV EIAV9	785-828	
PENV EIACV	785-828	
PENV EIAVW	785-828	
PENV EIAVY	785-828	
PENV FIVE	128-166	
PENV FIVT2	46-74	
PENV FLVGL	447-475	
PENV FLVLB	487-495	
PENV FLVSA	444-472	
PENV FOAMV	44-78	481-519
PENV FBSFB	315-350	
PENV FS1/9A	467-495	
PENV FS1/9B	447-475	
PENV FS1/9M	450-478	
PENV FB/ST	467-485	
PENV GALV	619-654	
PENV HV1A2	728-782	
PENV HV1B1	730-783	
PENV HV1BB	725-768	
PENV HV1BN	743-781	
PENV HV1BR	735-768	
PENV HV1C4	742-775	
PENV HV1EL	254-285	727-780
PENV HV1H2	730-783	
PENV HV1H3	730-783	
PENV HV1J3	741-774	
PENV HV1JR	722-766	
PENV HV1K3	662-686	762-780
PENV HV1MA	268-289	733-768
PENV HV1MF	728-761	
PENV HV1MN	392-430	731-764
PENV HV1ND	248-279	
PENV HV1OY	729-782	
PENV HV1PV	730-783	
PENV HV1RH	739-772	
PENV HV18C	739-783	

PENV_HV1W1	730-763
PENV_HV1W2	721-764
PENV_HV1Z2	264-285
PENV_HV1Z3	260-281
PENV_HV1Z8	265-286
PENV_HV1Z8	285-286
PENV_HV2BE	781-811
PENV_HV2D1	772-802
PENV_HV2G1	772-802
PENV_HV2NZ	777-814
PENV_HV2SB	743-776
PENV_JSRV	289-332
PENV_MMTV8	436-472
PENV_MMTV9	436-472
PENV_RSVP	533-570
PENV_SFV1	44-78
PENV_SFV3L	48-82
PENV_SIVCZ	745-778
PENV_SIVGB	247-277
PENV_SIVM1	788-800
PENV_SIVMK	785-789
PENV_SIVML	611-645
PENV_SIVS4	468-486
PENV_SIVSP	482-490
PHENA_CDVO	200-234
PHENA_IABUD	23-55
PHENA_JACKA	23-55
PHENA_JACKV	617-647
PHENA_IADA1	23-55
PHENA_IADC2	23-55
PHENA_IADH6	283-323
PHENA_IADN2	23-55
PHENA_IAPR	16-51
PHENA_IAGRE	23-55
PHENA_IAMAA	22-54
PHENA_IAMAB	27-59
PHENA_IARUD	23-56
PHENA_IASE2	23-55
PHENA_IASTA	617-647
PHENA_MUMPM	19-52
PHENA_MUMPR	19-52
PHENA_MUMPS	19-52
PHENA_NDVA	80-88
PHENA_NDVB	60-88
PHENA_NDVD	60-88
PHENA_NDVH	60-88
PHENA_NDVI	60-88

PHEMA NDVM	60-88
PHEMA NDVQ	60-88
PHEMA NDVTG	60-88
PHEMA NDVU	60-88
PHEMA PI1HW	28-80
PHEMA PI2H	13-48
PHEMA PI2HT	13-48
PHEMA PI3B	194-231
PHEMA PI3H4	194-231
PHEMA PI3HA	194-231
PHEMA PI3HT	194-231
PHEMA PI3HU	194-231
PHEMA PI3HV	194-231
PHEMA PI3HW	194-231
PHEMA PI3HX	194-231
PHEMA PI4HA	245-280
PHEMA RACVI	255-293
PHEMA RINDL	282-313
PHEMA SEND6	16-54
PHEMA SENDF	16-54
PHEMA SENDH	16-54
PHEMA SENDJ	16-54
PHEMA SENDZ	23-54
PHEMA 6V41	66-84
PHEMA 8V5	7-35
PHEMA 8V6CM	7-41
PHEMA SV6CP	7-41
PHEMA 8V6LN	7-35
PHEMA_VACCC	268-294
PHEMA_VACCI	268-294
PHEMA_VACCT	268-294
PHEMA_VACCV	268-294
PVENV BEV	18-51
PVENV DHV11	297-335
PVENV MCV1	203-238
PVENV MCV2	203-238
PVENV VACCC	208-241
PVENV VACCI	208-241
PVENV_VACCP	208-241
PVENV_VACCV	208-241
PVF03_VACCC	2-40
PVF03_VACCV	2-40
PVF11_FOWPV	297-330
PVF14_FOWPV	237-267
PVF7_CAPVK	89-118
PVF15_VACCC	28-81
PVF15_VACCV	28-81

PV001	HSV1	317-348		
PV002	HSV2	163-198		
PV002	VACCV	92-120		
PV002	VARV	92-120		
PV003	HSV1	108-138		
PV006	HSV1	54-83		
PV006	VACCC	99-136		
PV006	VARV	98-136		
PV007	VACCC	113-145		
PV007	VARV	113-145		
PV008	VACCC	303-338		
PV008	VACCV	286-301		
PV008	VARV	303-338		
PV011	HSV1	150-183		
PV012	HSV1	208-249		
PV012	HSVSA	68-108		
PV01	SPV1R	254-282	303-337	414-462
PV022	HSV1	300-337	647-678	
PV023	HSV1	70-108		
PV026	HSV1	94-125		
PV027	HSVSA	36-74		
PV028	HBV1	491-521		
PV028	HSVSA	7-40		
PV028	AMEPV	180-217		
PV02	SPV4	209-244		
PV035	HSV1	15-48	180-228	
PV036	HSVSA	151-185		
PV038	HSV1	543-577	848-882	
PV040	HSVSA	187-218		
PV041	HSV1	11-45	202-233	
PV042	HSV1	91-125		
PV043	HSV1	108-140	167-185	
PV046	HSV1	688-925		
PV048	HSVSA	329-367		
PV050	HSVSA	113-141		
PV051	HSV1	28-64	84-120	
PV052	HSV1	98-134		
PV055	HSV1	100-129		
PV056	HSV1	631-867	1081-1128	
PV056	HSV1	342-375	490-509	
PV058	HSVSA	25-60	105-233	
PV059	HSV1	82-118		
PV061	HSV1	76-109		
PV064	HSV1	56-89	393-401	420-452
PV065	HSV1	801-836	1280-1328	
PV067	HSV1	1560-188	1160-1185	
PV068	SPV1R	60-89		

PVG71 HSV5A	128-168			
PVG72 HSV1	445-478	720-761	1158-1189	1252-1285
PVG75 HSV1	263-281	387-422		
PVG78 HSV1	187-221			
PVG7 SPVIR	18-48			
PVG7-1BVB	1718-1747	1856-1891	2108-2148	3601-3633
PVG93 HCMVA	80-115	157-186		
PVG92 CVBF	1259-1294			
PVG92 CVBL9	681-681	1258-1294		
PVG92 CVBLY		1258-1294		
PVG92 CVBM		1258-1294		
PVG92 CVBQ		1258-1294		
PVG92 CVBV		1258-1294		
PVG92 CVH22	1053-1088			
PVG92 CVM4	1287-1304			
PVG92 CVMA5	1215-1252			
PVG92 CVMAH	1126-1163			
PVG92 CVPF8	632-665	738-784	1328-1363	
PVG92 CVPPU	630-663	734-762	1328-1361	
PVG92 CVPRB	512-540	1104-1139		
PVG92 CVPRM	408-441	1104-1139		
PVG92 FIPV	635-668	738-767	1331-1366	
PVG92 IBVB	163-188			
PVG9B HCMVA	116-147	708-743		
PVG9B HCMVT	116-147	707-744		
PVG9B HSV4U	72-110			
PVG9B HSV81	264-288			
PVG9B HSV82	264-289	745-774		
PVG9B HSVBC	203-287			
PVG9B ILTV8	442-472			
PVG9B ILTV8	452-482			
PVG9B ILTV7	462-482			
PVG9B MCMVS	135-163	738-776		
PVG9C HSV11	467-500			
PVG9C HSVIK	467-500			
PVG9C HSV2	435-466			
PVG9C HSV23	436-466			
PVG9C HSVBC	476-507			
PVG9C V21D	361-388	613-548		
PVG9C V21S	361-388	513-548		
PVG9D HSVEA	340-370			
PVG9D HSVFB	41-70	380-420		
PVG9D HSVFK	41-70	380-420		
PVG9E HSV4	96-126			
PVG9E HSV8B	63-100	380-420		
PVG9E HSVEL	63-100	382-422		
PVG9E PRVRI	332-368			

PVGLF_BRSVA	265-301	482-511
PVGLF_BRSVC	484-513	
PVGLF_BRSVR	484-513	
PVGLF_CDVO	562-588	
PVGLF_HRSV1	484-513	
PVGLF_HRSVA	484-513	
PVGLF_HRSVL	484-513	
PVGLF_HRSVR	484-513	
PVGLF_MEASE	224-266	451-484
PVGLF_MEASI	227-268	451-487
PVGLF_MEASY	224-268	451-484
PVGLF_MUMPM	446-474	
PVGLF_MUMPR	446-474	
PVGLF_MUMPS	5-38	448-474
PVGLF_NDVI	132-165	
PVGLF_PHODY	531-586	
PVGLF_P11HC	468-484	
PVGLF_P13B	453-481	
PVGLF_P13H4	463-481	
PVGLF_RINDK	220-252	447-480
PVGLF_RINDL	220-252	447-480
PVGLF_SENDS	480-488	
PVGLF_SENDF	480-488	
PVGLF_SENDH	480-488	
PVGLF_SENDJ	480-488	
PVGLF_SENDZ	480-488	
PVGLF_SV6	448-474	
PVGLF_TRTV	462-481	
PVGLG_HSVEB	327-384	
PVGLG_SYNV	524-553	
PVGLG_VSVIQ	450-488	
PVGLG_VBVJO	457-482	
PVGLG_VSVO	450-488	
PVGLG_VSVSJ	450-488	
PVGLH_HCMVA	691-719	
PVGLH_HCMVT	690-718	
PVGLH_HSVBG	640-877	
PVGLH_HVE4	814-850	
PVGLH_HSVEB	807-843	
PVGLI_HCMVA	168-194	
PVGLM_BUING	197-227	438-468
PVGLM_BUNL7	190-220	
PVGLM_BUNSH	190-220	344-381
PVGLM_BUNYV	183-228	434-472
PVGLM_DUGBV	244-273	637-672
PVGLM_HANTB	610-841	1081-1119
PVGLM_HANTH	188-222	1082-1120

PVGLM_HANTL	188-222	612-613	1083-1121
PVGLM_HANTV	188-222	612-613	1083-1121
PVGLM_PHV	616-849	1088-1121	
PVALM_PTPV	949-982	1275-1308	
PVGLM_PUUMH	620-853	1092-1125	
PVGLM_PUUMS	620-853	1092-1125	
PVGLM_RVFV	620-853	830-883	
PVGLM_RVFVZ	620-853	830-883	1168-1186
PVGLM_SEOUR	605-841	1082-1120	
PVGLM_SEOUS	610-841	1081-1119	
PVGLM_UUK	431-488	966-995	
PVGLP_BEV	1491-1526		
PVGLY_JUNIN	12-46		
PVGLY_LAS68	237-285		
PVGLY_LASSJ	238-288		
PVGLY_PIARV	12-50		
PVGLY_TACV	12-50		
PVGLY_TACV6	12-50	89-124	
PVGLY_TACV7	12-50	89-124	
PVGLY_TACVT	12-50	89-124	
PVGNB_CPMV	1627-1686		
PVGNM_BPMV	137-167	280-327	837-888
PVGNM_CPMV	209-242	741-771	
PVGNM_CPSMV	50-86	478-515	
PVGNM_RCMV	786-799		
PVGP2_EBV	7B-111		
PVGP3_EBV	7B-111		
PVMI_4EOV0	280-318	324-381	
PVMI_4EOV1	280-318		
PVMI_4EOV2	168-188		
PVM22_4EOV0	168-188		
PVM2_4EOV1	168-189		
PVM2_4EOV2	168-189		
PVM3_4EOV0	333-384		
PVMAT_SV5	308-342		
PVMAT_TRTV	122-160		
PVME1_CVBM	84-102		
PVME1_CVHOC	84-102		
PVME1_CVMA5	85-103		
PVME1_CVMJH	85-103		
PVME1_CVTKE	84-102		
PVMEM_EBV	178-213		
PVMP_CERV	93-126		
PVMP_SOCMV	86-98	273-303	
PVMSA_HPDB	201-238	268-302	
PVMSA_HPDC	194-227	288-301	
PVMSA_HPDU	167-180	231-284	

PVMSA_HPBWD	194-227	269-302
PVMSA_HPBGS	209-243	271-307
PVMSA_HPBHE	169-195	235-269
PVMSA_HPBVO	70-98	
PVMSA_HPBV2	244-272	
PVMSA_HPBV4	244-272	
PVMSA_HPBV9	244-272	
PVMSA_HPBVA	233-261	
PVMSA_HPBVD	70-98	
PVMSA_HPBVI	233-281	
PVMSA_HPBVJ	233-281	
PVMSA_HPBVL	233-281	
PVMSA_HPBVN	70-98	
PVMSA_HPBVO	233-281	
PVMSA_HPBVP	244-272	
PVMSA_HPBVR	244-272	
PVMSA_HPBVS	70-98	
PVMSA_HPBVW	233-281	
PVMSA_HPBVY	233-281	
PVMSA_HPBVZ	233-281	
PVMSA_WHV1	207-241	269-305
PVMSA_WHV58	212-246	274-310
PVMSA_WHV7	212-246	274-310
PVMSA_WHV8	212-246	274-310
PVMSA_WHV8I	212-246	274-310
PVMSA_WHVW8	125-181	
PVMT2_I2I1	10-44	
PVMT2_MXVL	6-34	141-170
PVMT9_MXVL	246-282	

5.3. SYNTHESIS OF PEPTIDES

The peptides of the invention may be synthesized or prepared by techniques well known in the art. See, for example, Creighton, 1983, *Proteins: Structures and Molecular Principles*, W.H. Freeman and Co., NY, 5 which is incorporated herein by reference in its entirety. Short peptides, for example, can be synthesized on a solid support or in solution. Longer peptides may be made using recombinant DNA techniques. Here, the nucleotide sequences encoding the peptides 10 of the invention may be synthesized, and/or cloned, and expressed according to techniques well known to those of ordinary skill in the art. See, for example, Sambrook, *et al.*, 1989, *Molecular Cloning, A Laboratory Manual*, Vols. 1-3, Cold Spring Harbor 15 Press, NY.

The peptides of the invention may alternatively be synthesized such that one or more of the bonds which link the amino acid residues of the peptides are non-peptide bonds. These alternative non-peptide 20 bonds may be formed by utilizing reactions well known to those in the art, and may include, but are not limited to imino, ester, hydrazide, semicarbazide, and azo bonds, to name but a few. In yet another embodiment of the invention, peptides comprising the 25 sequences described above may be synthesized with additional chemical groups present at their amino and/or carboxy termini, such that, for example, the stability, bioavailability, and/or inhibitory activity of the peptides is enhanced. For example, hydrophobic 30 groups such as carbobenzoyl, dansyl, or t-butylloxycarbonyl groups, may be added to the peptides' amino termini. Likewise, an acetyl group or a 9-fluorenylmethoxy-carbonyl group may be placed at the 35 peptides' amino termini. (See "X" in Tables I to IV, above.) Additionally, the hydrophobic group, t-

butyloxycarbonyl, or an amido group may be added to the peptides' carboxy termini. (See "Z" in Tables I to IV, above.) Further, the peptides of the invention may be synthesized such that their steric configuration is altered. For example, the D-isomer 5 of one or more of the amino acid residues of the peptide may be used, rather than the usual L-isomer. Still further, at least one of the amino acid residues 10 of the peptides of the invention may be substituted by one of the well known non-naturally occurring amino acid residues. Alterations such as these may serve to increase the stability, bioavailability and/or inhibitory action of the peptides of the invention.

Any of the peptides described above may, 15 additionally, have a non-peptide macromolecular carrier group covalently attached to their amino and/or carboxy termini. Such macromolecular carrier groups may include, for example, lipid-fatty acid conjugates, polyethylene glycol, or carbohydrates. "X", in Tables I to IV, above, may therefore 20 additionally represent any of the above macromolecular carrier groups covalently attached to the amino terminus of a peptide. Likewise, "Z", in Tables I to IV, may additionally represent any of the 25 macromolecular carrier groups described above.

5.4. ASSAYS FOR ANTIVIRAL ACTIVITY

The antiviral activity exhibited by the peptides of the invention may be measured, for example, by 30 easily performed in vitro assays, such as those described below, which can test the peptides' ability to inhibit syncytia formation, or their ability to inhibit infection by cell-free virus. Using these assays, such parameters as the relative antiviral 35 activity of the peptides, exhibit against a given strain of virus and/or the strain specific inhibitory

activity of the peptide can be determined. A cell fusion assay may be utilized to test the peptides' ability to inhibit HIV-induced syncytia formation in vitro. Such an assay may comprise culturing uninfected CD-4⁺ cells (such as Molt or CEM cells, for 5 example) in the presence of chronically HIV-infected cells and a peptide to be assayed. For each peptide, a range of peptide concentrations may be tested. This range should include a control culture wherein no peptide has been added. Standard conditions for 10 culturing, well known to those of ordinary skill in the art, are used. After incubation for an appropriate period (24 hours at 37°C, for example) the culture is examined microscopically for the presence of multinucleated giant cells, which are indicative of 15 cell fusion and syncytia formation.

A reverse transcriptase (RT) assay may be utilized to test the peptides' ability to inhibit infection of CD-4⁺ cells by cell-free HIV. Such an assay may comprise culturing an appropriate 20 concentration (i.e., TCID₅₀) of virus and CD-4⁺ cells in the presence of the peptide to be tested. Culture conditions well known to those in the art are used. As above, a range of peptide concentrations may be used, in addition to a control culture wherein no 25 peptide has been added. After incubation for an appropriate period (e.g., 7 days) of culturing, a cell-free supernatant is prepared, using standard procedures, and tested for the present of RT activity as a measure of successful infection. The RT activity 30 may be tested using standard techniques such as those described by, for example, Goff et al. (Goff, S. et al., 1981, J. Virol. 38:239-248) and/or Willey et al. (Willey, R. et al., 1988, J. Virol. 62:139-147). These references are incorporated herein by reference 35 in their entirety.

Standard methods which are well-known to those of skill in the art may be utilized for assaying non-retroviral activity. See, for example, Pringle et al. (Pringle, C.R. et al., 1985, J. Medical Virology 17:377-386) for a discussion of respiratory syncytial virus and parainfluenza virus activity assay techniques. Further, see, for example, "Zinsser Microbiology", 1988, Joklik, W.K. et al., eds., Appleton & Lange, Norwalk, CT, 19th ed., for a general review of such techniques. These references are incorporated by reference herein in its entirety.

5.5. USES OF THE PEPTIDES OF THE INVENTION

The DP-178 (SEQ ID:1) peptides of the invention, and DP-178 fragments, analogs, and homologs, exhibit potent antiviral activity. The DP-107-like and DP-178-like peptides of the invention preferably exhibit antiviral activity. As such, the peptides may be used as inhibitors of human and non-human viral and retroviral, especially HIV, transmission to uninfected cells.

The human retroviruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to all strains of HIV-1 and HIV-2 and the human T-lymphocyte viruses (HTLV-I and II). The non-human retroviruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to bovine leukosis virus, feline sarcoma and leukemia viruses, simian immunodeficiency, sarcoma and leukemia viruses, and sheep progressive pneumonia viruses.

Non retroviral viruses whose transmission may be inhibited by the peptides of the invention include, but are not limited to human respiratory syncytial virus, canine distemper virus, newcastle disease virus, human parainfluenza virus, and influenza

viruses. Further, any virus or retrovirus containing peptides listed in Tables V through X above, may be inhibited by the peptides of the invention.

As discussed more fully, below, in Section 5.5.1 and in the Example presented, below, in Section 8, DP-
5 107 and DP-178, and DP-107-like and DP-178-like peptides form non-covalent protein-protein interactions which are required for normal activity of the virus. Thus, the peptides of the invention may also be utilized as components in assays for the
10 15 identification of compounds that interfere with such protein-protein interactions and may, therefore, act as antiviral agents. These assays are discussed, below, in Section 5.5.1.

15 5.5.1. ANTIVIRAL COMPOUND SCREENING SCREENING ASSAYS FOR COMPOUNDS THAT INTERACT WITH THE PKD1 GENE PRODUCT

As demonstrated in the Example presented in Section 8, below, DP-107 and DP-178 portions of the TM
20 25 protein gp41 form non-covalent protein-protein interactions. As also demonstrated, the maintenance of such interactions is necessary for normal viral infectivity. Thus, compounds which bind DP-107, bind DP-178, and/or act to disrupt normal DP-107/DP-178 protein-protein interactions may act as patent
30 35 antiviral agents. Described below are assays for the identification of such compounds. Note that, while, for ease and clarity of discussion, DP-107 and DP-178 peptides will be used as components of the assays described, but it is to be understood that any of the DP-107-like or DP-178-like peptides described, above, in Sections 5.1 and 5.2 may also be utilized as part of these screens for antiviral compounds.

Compounds which may be tested for an ability to bind DP-107, DP-178, and/or disrupt DP-107/DP-178 interactions, and which therefore, potentially

represent antiviral compounds, include, but are not limited to, peptides made of D- and/or L-configuration amino acids (in, for example, the form of random peptide libraries; see Lam, K.S. et al., 1991, *Nature* 354:82-84), phosphopeptides (in, for example, the form of random or partially degenerate, directed phosphopeptide libraries; see, for example, Songyang, Z. et al., 1993, *Cell* 72:767-778), antibodies, and small organic or inorganic molecules. Synthetic compounds, natural products, and other sources of potentially effective materials may be screened in a variety of ways, as described in this Section. The compounds, antibodies, or other molecules identified may be tested for an ability to inhibit viral activity, utilizing, for example, viral assays such as those described, above, in Section 5.4.

Among the peptides which may be tested are soluble peptides comprising DP-107 and/or DP-178 domains, and peptides comprising DP-107 and/or DP-178 domains having one or more mutations within one or both of the domains, such as the M41-P peptide described, below, in the Example presented in Section 8, which contains a isoleucine to proline mutation within the DP-178 sequence.

In one embodiment of such screening methods is a method for identifying a compound to be tested for antiviral ability comprising:

- (a) exposing at least one compound to a peptide comprising a DP-107 peptide for a time sufficient to allow binding of the compound to the DP-107 peptide;
- (b) removing non-bound compounds; and
- (c) determining the presence of the compound bound to the DP-107 peptide, thereby identifying an agent to be tested for antiviral ability.

In a second embodiment of such screening methods is a method for identifying a compound to be tested for antiviral ability comprising:

- (a) exposing at least one compound to a peptide comprising a DP-178 peptide for a time 5 sufficient to allow binding of the compound to the DP-178 peptide;
- (b) removing non-bound compounds; and
- (c) determining the presence of the compound bound to the DP-178 peptide, 10 thereby identifying an agent to be tested for antiviral ability.

One method utilizing these types of approaches that may be pursued in the isolation of such DP-107-binding or DP-178-binding compounds is an assay which 15 would include the attachment of either the DP-107 or the DP-178 peptide to a solid matrix, such as, for example, agarose or plastic beads, microtiter plate wells, petri dishes, or membranes composed of, for example, nylon or nitrocellulose. In such an assay 20 system, either the DP-107 or DP-178 protein may be anchored onto a solid surface, and the compound, or test substance, which is not anchored, is labeled, either directly or indirectly. In practice, 25 microtiter plates are conveniently utilized. The anchored component may be immobilized by non-covalent or covalent attachments. Non-covalent attachment may be accomplished simply by coating the solid surface with a solution of the protein and drying.

Alternatively, an immobilized antibody, preferably a 30 monoclonal antibody, specific for the protein may be used to anchor the protein to the solid surface. The surfaces may be prepared in advance and stored.

In order to conduct the assay, the labeled compound is added to the coated surface containing the 35 anchored DP-107 or DP-178 peptide. After the reaction

is complete, unreacted components are removed (e.g., by washing) under conditions such that any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways.

5 Where the compound is pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the labeled component is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using 10 a labeled antibody specific for the compound (the antibody, in turn, may be directly labeled or indirectly labeled with a labeled anti-Ig antibody).

Alternatively, such an assay can be conducted in a liquid phase, the reaction products separated from 15 unreacted components, and complexes detected; e.g., using an immobilized antibody specific for DP-107 or DP-178, whichever is appropriate for the given assay, or ab antibody specific for the compound, i.e., the test substance, in order to anchor any complexes 20 formed in solution, and a labeled antibody specific for the other member of the complex to detect anchored complexes.

By utilizing procedures such as this, large 25 numbers of types of molecules may be simultaneously screened for DP-107 or DP-178-binding capability, and thus potential antiviral activity.

Further, compounds may be screened for an ability to inhibit the formation of or, alternatively, disrupt 30 DP-107/DP-178 complexes. Such compounds may then be tested for antiviral capability. For ease of description, DP-107 and DP-178 will be referred to as "binding partners." Compounds that disrupt such interactions may exhibit antiviral activity. Such compounds may include, but are not limited to

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molecules such as antibodies, peptides, and the like described above.

The basic principle of the assay systems used to identify compounds that interfere with the interaction between the DP-107 and DP-178 peptides involves
5 preparing a reaction mixture containing peptides under conditions and for a time sufficient to allow the two peptides to interact and bind, thus forming a complex. In order to test a compound for disruptive activity, the reaction is conducted in the presence and absence
10 of the test compound, i.e., the test compound may be initially included in the reaction mixture, or added at a time subsequent to the addition of one of the binding partners; controls are incubated without the test compound or with a placebo. The formation of any
15 complexes between the binding partners is then detected. The formation of a complex in the control reaction, but not in the reaction mixture containing the test compound indicates that the compound interferes with the interaction of the DP-107 and
20 DP-178 peptides.

The assay for compounds that interfere with the interaction of the binding partners can be conducted in a heterogeneous or homogeneous format. Heterogeneous assays involve anchoring one of the
25 binding partners onto a solid phase and detecting complexes anchored on the solid phase at the end of the reaction. In homogeneous assays, the entire reaction is carried out in a liquid phase. In either approach, the order of addition of reactants can be
30 varied to obtain different information about the compounds being tested. For example, test compounds that interfere with the interaction between the binding partners, e.g., by competition, can be identified by conducting the reaction in the presence
35 of the test substance; i.e., by adding the test

substance to the reaction mixture prior to or simultaneously with the binding partners. On the other hand, test compounds that disrupt preformed complexes, e.g. compounds with higher binding constants that displace one of the binding partners 5 from the complex, can be tested by adding the test compound to the reaction mixture after complexes have been formed. The various formats are described briefly below.

10 In a heterogeneous assay system, one binding partner, e.g., either the DP-107 or DP-178 peptide, is anchored onto a solid surface, and its binding partner, which is not anchored, is labeled, either directly or indirectly. In practice, microtiter plates are conveniently utilized. The anchored 15 species may be immobilized by non-covalent or covalent attachments. Non-covalent attachment may be accomplished simply by coating the solid surface with a solution of the protein and drying. Alternatively, an immobilized antibody specific for the protein may 20 be used to anchor the protein to the solid surface. The surfaces may be prepared in advance and stored.

25 In order to conduct the assay, the binding partner of the immobilized species is added to the coated surface with or without the test compound. After the reaction is complete, unreacted components 30 are removed (e.g., by washing) and any complexes formed will remain immobilized on the solid surface. The detection of complexes anchored on the solid surface can be accomplished in a number of ways. 35 Where the binding partner was pre-labeled, the detection of label immobilized on the surface indicates that complexes were formed. Where the binding partner is not pre-labeled, an indirect label can be used to detect complexes anchored on the surface; e.g., using a labeled antibody specific for

the binding partner (the antibody, in turn, may be directly labeled or indirectly labeled with a labeled anti-Ig antibody). Depending upon the order of addition of reaction components, test compounds which inhibit complex formation or which disrupt preformed complexes can be detected.

Alternatively, the reaction can be conducted in a liquid phase in the presence or absence of the test compound, the reaction products separated from unreacted components, and complexes detected; e.g., using an immobilized antibody specific for one binding partner to anchor any complexes formed in solution, and a labeled antibody specific for the other binding partner to detect anchored complexes. Again, depending upon the order of addition of reactants to the liquid phase, test compounds which inhibit complex or which disrupt preformed complexes can be identified.

In an alternate embodiment of the invention, a homogeneous assay can be used. In this approach, a preformed complex of the DP-107 and DP-178 peptides is prepared in which one of the binding partners is labeled, but the signal generated by the label is quenched due to complex formation (see, e.g., U.S. Patent No. 4,109,496 by Rubenstein which utilizes this approach for immunoassays). The addition of a test substance that competes with and displaces one of the binding partners from the preformed complex will result in the generation of a signal above background. In this way, test substances which disrupt DP-107/DP-178 protein-protein interaction can be identified.

5.5 PHARMACEUTICAL FORMULATIONS, DOSAGES AND MODES OF ADMINISTRATION

With respect to HIV, the peptides of the invention may be used as a therapeutic in the

treatment of AIDS. The peptides of the invention may be administered using techniques well known to those in the art. Preferably, agents are formulated and administered systemically. Techniques for formulation and administration may be found in "Remington's 5 Pharmaceutical Sciences", 18th ed., 1990, Mack Publishing Co., Easton, PA. Suitable routes may include oral, rectal, transmucosal, or intestinal administration; parenteral delivery, including intramuscular, subcutaneous, intramedullary 10 injections, as well as intrathecal, direct intraventricular, intravenous, intraperitoneal, intranasal, or intraocular injections, just to name a few. Most preferably, administration is intravenous. For injection, the agents of the invention may be 15 formulated in aqueous solutions, preferably in physiologically compatible buffers such as Hanks' solution, Ringer's solution, or physiological saline buffer. For such transmucosal administration, penetrants appropriate to the barrier to be permeated 20 are used in the formulation. Such penetrants are generally known in the art.

In addition, the peptides may be used as a prophylactic measure in previously uninfected 25 individuals after acute exposure to an HIV virus. Examples of such prophylactic use of the peptides may include, but are not limited to, prevention of virus transmission from mother to infant and other settings where the likelihood of HIV transmission exists, such as, for example, accidents in health care settings 30 wherein workers are exposed to HIV-containing blood products. The peptides of the invention in such cases may serve the role of a prophylactic vaccine, wherein the host raises antibodies against the peptides of the invention, which then serve to neutralize HIV viruses 35 by, for example, inhibiting further HIV infection.

Administration of the peptides of the invention as a prophylactic vaccine, therefore, would comprise administering to a host a concentration of peptides effective in raising an immune response which is sufficient to neutralize HIV, by, for example, 5 inhibiting HIV ability to infect cells. The exact concentration will depend upon the specific peptide to be administered, but may be determined by using standard techniques for assaying the development of an immune response which are well known to those of 10 ordinary skill in the art. The peptides to be used as vaccines are usually administered intramuscularly.

The peptides may be formulated with a suitable adjuvant in order to enhance the immunological response. Such adjuvants may include, but are not 15 limited to mineral gels such as aluminum hydroxide; surface active substances such as lysolecithin, pluronic polyols, polyanions; other peptides; oil emulsions; and potentially useful human adjuvants such as BCG and *Corynebacterium parvum*. Many methods may 20 be used to introduce the vaccine formulations described here. These methods include but are not limited to oral, intradermal, intramuscular, intraperitoneal, intravenous, subcutaneous, and intranasal routes.

25 Alternatively, an effective concentration of polyclonal or monoclonal antibodies raised against the peptides of the invention may be administered to a host so that no uninfected cells become infected by HIV. The exact concentration of such antibodies will 30 vary according to each specific antibody preparation, but may be determined using standard techniques well known to those of ordinary skill in the art. Administration of the antibodies may be accomplished using a variety of techniques, including, but not 35 limited to those described in this section.

Effective dosages of the peptides of the invention to be administered may be determined through procedures well known to those in the art which address such parameters as biological half-life, bioavailability, and toxicity. Given the data 5 presented below in Section 6, DP-178, for example, may prove efficacious in vivo at doses required to achieve circulating levels of 10ng per ml of peptide.

A therapeutically effective dose refers to that amount of the compound sufficient to result in 10 amelioration of symptoms or a prolongation of survival in a patient. Toxicity and therapeutic efficacy of such compounds can be determined by standard pharmaceutical procedures in cell cultures or experimental animals, e.g., for determining the LD50 15 (the dose lethal to 50% of the population) and the ED50 (the dose therapeutically effective in 50% of the population). The dose ratio between toxic and therapeutic effects is the therapeutic index and it can be expressed as the ratio LD50/ED50. Compounds 20 which exhibit large therapeutic indices are preferred. The data obtained from these cell culture assays and animal studies can be used in formulating a range of dosage for use in humans. The dosage of such compounds lies preferably within a range of 25 circulating concentrations that include the ED50 with little or no toxicity. The dosage may vary within this range depending upon the dosage form employed and the route of administration utilized. For any compound used in the method of the invention, the 30 therapeutically effective dose can be estimated initially from cell culture assays. A dose may be formulated in animal models to achieve a circulating plasma concentration range that includes the IC50 (i.e., the concentration of the test compound which 35 achieves a half-maximal disruption of the PTK/adaptor

protein complex, or a half-maximal inhibition of the cellular level and/or activity of a complex component) as determined in cell culture. Such information can be used to more accurately determine useful doses in humans. Levels in plasma may be measured, for 5 example, by high performance liquid chromatography (HPLC).

The exact formulation, route of administration and dosage can be chosen by the individual physician in view of the patient's condition. (See e.g. Fingl 10 et al., 1975, in "The Pharmacological Basis of Therapeutics", Ch. 1 p1).

It should be noted that the attending physician would know how to and when to terminate, interrupt, or adjust administration due to toxicity, or to organ 15 dysfunctions. Conversely, the attending physician would also know to adjust treatment to higher levels if the clinical response were not adequate (precluding toxicity). The magnitude of an administrated dose in the management of the oncogenic disorder of interest 20 will vary with the severity of the condition to be treated and to the route of administration. The dose and perhaps dose frequency, will also vary according to the age, body weight, and response of the individual patient. A program comparable to that 25 discussed above may be used in veterinary medicine.

As demonstrated in the Example presented below in Section 6, the antiviral activity of the peptides of the invention may show a pronounced type and subtype 30 specificity, i.e., specific peptides may be effective in inhibiting the activity of only specific viruses. This feature of the invention presents many advantages. One such advantage, for example, lies in the field of diagnostics, wherein one can use the 35 antiviral specificity of the peptide of the invention to ascertain the identity of a viral isolate. With

respect to HIV, one may easily determine whether a viral isolate consists of an HIV-1 or HIV-2 strain. For example, uninfected CD-4⁺ cells may be co-infected with an isolate which has been identified as containing HIV the DP-178 (SEQ ID:1) peptide, after 5 which the retroviral activity of cell supernatents may be assayed, using, for example, the techniques described above in Section 5.2. Those isolates whose retroviral activity is completely or nearly completely inhibited contain HIV-1. Those isolates whose viral 10 activity is unchanged or only reduced by a small amount, may be considered to not contain HIV-1. Such an isolate may then be treated with one or more of the other DP-178 peptides of the invention, and subsequently be tested for its viral activity in order 15 to determine the identify of the viral isolate.

Use of pharmaceutically acceptable carriers to formulate the compounds herein disclosed for the practice of the invention into dosages suitable for systemic administration is within the scope of the 20 invention. With proper choice of carrier and suitable manufacturing practice, the compositions of the present invention, in particular, those formulated as solutions, may be administered parenterally, such as by intravenous injection. The compounds can be 25 formulated readily using pharmaceutically acceptable carriers well known in the art into dosages suitable for oral administration. Such carriers enable the compounds of the invention to be formulated as tablets, pills, capsules, liquids, gels, syrups, 30 slurries, suspensions and the like, for oral ingestion by a patient to be treated.

Pharmaceutical compositions suitable for use in the present invention include compositions wherein the active ingredients are contained in an effective 35 amount to achieve its intended purpose. Determination

of the effective amounts is well within the capability of those skilled in the art, especially in light of the detailed disclosure provided herein.

In addition to the active ingredients, these pharmaceutical compositions may contain suitable 5 pharmaceutically acceptable carriers comprising excipients and auxiliaries which facilitate processing of the active compounds into preparations which can be used pharmaceutically. The preparations formulated for oral administration may be in the form of tablets, 10 dragees, capsules, or solutions.

The pharmaceutical compositions of the present invention may be manufactured in a manner that is itself known, e.g., by means of conventional mixing, 15 dissolving, granulating, dragee-making, levigating, emulsifying, encapsulating, entrapping or lyophilizing processes.

Pharmaceutical formulations for parenteral administration include aqueous solutions of the active compounds in water-soluble form. Additionally, 20 suspensions of the active compounds may be prepared as appropriate oily injection suspensions. Suitable lipophilic solvents or vehicles include fatty oils such as sesame oil, or synthetic fatty acid esters, such as ethyl oleate or triglycerides, or liposomes. 25 Aqueous injection suspensions may contain substances which increase the viscosity of the suspension, such as sodium carboxymethyl cellulose, sorbitol, or dextran. Optionally, the suspension may also contain suitable stabilizers or agents which increase the 30 solubility of the compounds to allow for the preparation of highly concentrated solutions.

Pharmaceutical preparations for oral use can be obtained by combining the active compounds with solid excipient, optionally grinding a resulting mixture, 35 and processing the mixture of granules, after adding

suitable auxiliaries, if desired, to obtain tablets or dragee cores. Suitable excipients are, in particular, fillers such as sugars, including lactose, sucrose, mannitol, or sorbitol; cellulose preparations such as, for example, maize starch, wheat starch, rice starch, 5 potato starch, gelatin, gum tragacanth, methyl cellulose, hydroxypropylmethyl-cellulose, sodium carboxymethylcellulose, and/or polyvinylpyrrolidone (PVP). If desired, disintegrating agents may be added, such as the cross-linked polyvinyl pyrrolidone, 10 agar, or alginic acid or a salt thereof such as sodium alginate.

Dragee cores are provided with suitable coatings. For this purpose, concentrated sugar solutions may be used, which may optionally contain gum arabic, talc, 15 polyvinyl pyrrolidone, carbopol gel, polyethylene glycol, and/or titanium dioxide, lacquer solutions, and suitable organic solvents or solvent mixtures. Dyestuffs or pigments may be added to the tablets or dragee coatings for identification or to characterize 20 different combinations of active compound doses.

Pharmaceutical preparations which can be used orally include push-fit capsules made of gelatin, as well as soft, sealed capsules made of gelatin and a plasticizer, such as glycerol or sorbitol. The 25 push-fit capsules can contain the active ingredients in admixture with filler such as lactose, binders such as starches, and/or lubricants such as talc or magnesium stearate and, optionally, stabilizers. In soft capsules, the active compounds may be dissolved 30 or suspended in suitable liquids, such as fatty oils, liquid paraffin, or liquid polyethylene glycols. In addition, stabilizers may be added.

6. EXAMPLE: DP-178 (SEQ ID:1) IS A POTENT
INHIBITOR OF HIV-1 INFECTION

In this example, DP-178 (SEQ ID:1) is shown to be a potent inhibitor of HIV-1 mediated CD-4⁺ cell-cell fusion and infection by cell free virus. In the 5 fusion assay, this peptide completely blocks virus induced syncytia formation at concentrations of from 1-10 ng/ml. In the infectivity assay the inhibitory concentration is somewhat higher, blocking infection at 90ng/ml. It is further shown that DP-178 (SEQ 10 ID:1) shows that the antiviral activity of DP-178 (SEQ ID:1) is highly specific for HIV-1. Additionally, a synthetic peptide, DP-185 (SEQ ID:3), representing a HIV-1-derived DP-178 homolog is also found to block HIV-1-mediated syncytia formation.

15

6.1. MATERIALS AND METHODS

6.1.1. PEPTIDE SYNTHESIS

Peptides were synthesized using Fast Moc 20 chemistry on an Applied Biosystems Model 431A peptide synthesizer. Amidated peptides were prepared using Rink resin (Advanced Chemtech) while peptides containing free carboxy termini were synthesized on Wang (p-alkoxy-benzyl-alcohol) resin (Bachem). First 25 residues were double coupled to the appropriate resin and subsequent residues were single coupled. Each coupling step was followed by acetic anhydride capping. Peptides were cleaved from the resin by treatment with trifluoracetic acid (TFA) (10ml), H₂O 30 (0.5ml), thioanisole (0.5ml), ethanedithiol (0.25ml), and crystalline phenol (0.75g). Purification was carried out by reverse phase HPLC. Approximately 50mg samples of crude peptide were chromatographed on a Waters Delta Pak C18 column (19mm x 30cm, 15 μ 35 spherical) with a linear gradient; H₂O/acetonitrile

0.1% TFA. Lyophilized peptides were stored desiccated and peptide solutions were made in water at about 1mg/ml. Electrospray mass spectrometry yielded the following results: DP-178 (SEQ ID:1):4491.87 (calculated 4491.94); DP-180 (SEQ ID:2):4491.45 (calculated 4491.94); DP-185 (SEQ ID:3):not done (calculated 4546.97).

6.1.2. VIRUS

The HIV-1_{LAI} virus was obtained from R. Gallo (Popovic, M. *et al.*, 1984, *Science* 224:497-508) and propagated in CEM cells cultured in RPMI 1640 containing 10% fetal calf serum. Supernatant from the infected CEM cells was passed through a 0.2 μ m filter and the infectious titer estimated in a microinfectivity assay using the AA5 cell line to support virus replication. For this purpose, 25 μ l of serial diluted virus was added to 75 μ l AA5 cells at a concentration of 2×10^5 /ml in a 96-well microtitre plate. Each virus dilution was tested in triplicate. Cells were cultured for eight days by addition of fresh medium every other day. On day 8 post infection, supernatant samples were tested for virus replication as evidenced by reverse transcriptase activity released to the supernatant. The TCID₅₀ was calculated according to the Reed and Muench formula (Reed, L.J. *et al.*, 1938, *Am. J. Hyg.* 27:493-497). The titer of the HIV-1_{LAI} and HIV-1_{MN} stocks used for these studies, as measured on the AA5 cell line, was approximately 1.4×10^6 and 3.8×10^4 TCID₅₀/ml, respectively.

6.1.3. CELL FUSION ASSAY

Approximately 7×10^4 Molt cells were incubated with 1×10^4 CEM cells chronically infected with the HIV-1_{LAI} virus in 96-well plates (one-half area cluster plates; Costar, Cambridge, MA) in a final volume of

100 μ l culture medium as previously described (Matthews, T.J. *et al.*, 1987, Proc. Natl. Acad. Sci. USA 84: 5424-5428). Peptide inhibitors were added in a volume of 10 μ l and the cell mixtures were incubated for 24 hr. at 37°C. At that time, multinucleated 5 giant cells were estimated by microscopic examination at a 40x magnification which allowed visualization of the entire well in a single field.

10 6.1.4. CELL FREE VIRUS INFECTION ASSAY
15 Synthetic peptides were incubated at 37°C with either 247 TCID₅₀ (for experiment depicted in FIG. 2), or 62 TCID₅₀ (for experiment depicted in FIG. 3) units of HIV-1_{LAI} virus or 25 TCID₅₀ units of HIV-2_{NIH2} and CEM CD4⁺ cells at peptide concentrations of 0, 0.04, 0.4, 4.0, and 40 μ g/ml for 7 days. The resulting reverse transcriptase (RT) activity in counts per minute was determined using the assay described, below, in Section 6.1.5. See, Reed, L.J. *et al.*, 1938, Am. J. Hyg. 27: 493-497 for an explanation of TCID₅₀ 20 calculations.

15 6.1.5. REVERSE TRANSCRIPTASE ASSAY
20 The micro-reverse transcriptase (RT) assay was adapted from Goff *et al.* (Goff, S. *et al.*, 1981, J. Virol. 38:239-248) and Willey *et al.* (Willey, R. *et al.*, 1988, J. Virol. 62:139-147). Supernatants from 25 virus/cell cultures are adjusted to 1% Triton-X100. A 10 μ l sample of supernatant was added to 50 μ l of RT cocktail in a 96-well U-bottom microtitre plate and 30 the samples incubated at 37°C for 90 min. The RT cocktail contained 75mM KCl, 2mM dithiothreitol, 5mM MgCl₂, 5 μ g/ml poly A (Pharmacia, cat. No. 27-4110-01), 0.25 units/ml oligo dT (Pharmacia, cat. No. 27-7858-35 01), 0.05% NP40, 50mM Tris-HCl, pH 7.8, 0.5 μ M non-

radioactive dTTP, and 10 μ Ci/ml 32 P-dTTP (Amersham, cat. No. PB.10167).

After the incubation period, 40 μ l of reaction mixture was applied to a Schleicher and Schuell (S+S) NA45 membrane (or DE81 paper) saturated in 2 x SSC buffer (0.3M NaCl and 0.003M sodium citrate) held in a S+S Minifold over one sheet of GB003 (S+S) filter paper, with partial vacuum applied. Each well of the minifold was washed four times with 200 μ l 2xSSC, under full vacuum. The membrane was removed from the minifold and washed 2 more times in a pyrex dish with an excess of 2xSSC. Finally, the membrane was drained on absorbent paper, placed on Whatman #3 paper, covered with Saran wrap, and exposed to film overnight at -70°C.

15

6.2. RESULTS

6.2.1. PEPTIDE INHIBITION OF INFECTED CELL-INDUCED SYNCYTIA FORMATION

20 The initial screen for antiviral activity assayed peptides' ability to block syncytium formation induced by overnight co-cultivation of uninfected Molt4 cells with chronically HIV-1 infected CEM cells. The results of several such experiments are presented 25 herein. In the first of these experiments, serial DP-178 (SEQ ID:1) peptide concentrations between 10 μ g/ml and 12.5ng/ml were tested for blockade of the cell fusion process. For these experiments, CEM cells chronically infected with either HIV-1_{LAI}, HIV-1_{MN}, HIV-30 1_{RF}, or HIV-1_{SP2} virus were cocultivated overnight with uninfected Molt 4 cells. The results (FIG. 4) show that DP-178 (SEQ ID:1) afforded complete protection against each of the HIV-1 isolates down to the lowest concentration of DP-178 (SEQ ID:1) used. For HIV_{LAI} 35 inhibition, the lowest concentration tested was

12.5ng/ml; for all other HIV-1 viruses, the lowest concentration of DP-178 (SEQ ID:1) used in this study was 100ng/ml. A second peptide, DP-180 (SEQ ID:2), containing the same amino acid residues as DP-178 (SEQ ID:1) but arranged in a random order exhibited no 5 evidence of anti-fusogenic activity even at the high concentration of 40 μ g/ml (FIG. 4). These observations indicate that the inhibitory effect of DP-178 (SEQ ID:1) is primary sequence-specific and not related to 10 non-specific peptide/protein interactions. The actual endpoint (*i.e.*, the lowest effective inhibitory concentration) of DP-178 inhibitory action is within 15 the range of 1-10 ng/ml.

The next series of experiments involved the preparation and testing of a DP-178 (SEQ ID:1) homolog 15 for its ability to inhibit HIV-1-induced syncytia formation. As shown in FIG. 1, the sequence of DP-185 (SEQ ID:3) is slightly different from DP-178 (SEQ ID:1) in that its primary sequence is taken from the HIV-1_{SP2} isolate and contains several amino acid 20 differences relative to DP-178 (SEQ ID:1) near the N terminus. As shown in FIG. 4, DP-185 (SEQ ID:3), exhibits inhibitory activity even at 312.5ng/ml, the lowest concentration tested.

The next series of experiments involved a 25 comparison of DP-178 (SEQ ID:1) HIV-1 and HIV-2 inhibitory activity. As shown in FIG. 5, DP-178 (SEQ ID:1) blocked HIV-1-mediated syncytia formation at peptide concentrations below 1ng/ml. DP-178 (SEQ ID:1) failed, however, to block HIV-2 mediated 30 syncytia formation at concentrations as high as 10 μ g/ml. This striking 4 log selectivity of DP-178 (SEQ ID:1) as an inhibitor of HIV-1-mediated cell fusion demonstrates an unexpected HIV-1 specificity in 35 the action of DP-178 (SEQ ID:1). DP-178 (SEQ ID:1) inhibition of HIV-1-mediated cell fusion, but the

peptide's inability to inhibit HIV-2 mediated cell fusion in the same cell type at the concentrations tested provides further evidence for the high degree of selectivity associated with the antiviral action of DP-178 (SEQ ID:1).

5

6.2.2. PEPTIDE INHIBITION OF INFECTION BY CELL-FREE VIRUS

DP-178 (SEQ ID:1) was next tested for its ability to block CD-4⁺ CEM cell infection by cell free HIV-1 virus. The results, shown in FIG. 2, are from an experiment in which DP-178 (SEQ ID:1) was assayed for its ability to block infection of CEM cells by an HIV-1_{LAI} isolate. Included in the experiment were three control peptides, DP-116 (SEQ ID:9), DP-125 (SEQ ID:8), and DP-118 (SEQ ID:10). DP-116 (SEQ ID:9) represents a peptide previously shown to be inactive using this assay, and DP-125 (SEQ ID:8; Wild, C. *et al.*, 1992, Proc. Natl. Acad. Sci. USA 89:10,537) and DP-118 (SEQ ID:10) are peptides which have previously been shown to be active in this assay. Each concentration (0, 0.04, 0.4, 4, and 40 μ g/ml) of peptide was incubated with 247 TCID₅₀ units of HIV-1_{LAI} virus and CEM cells. After 7 days of culture, cell-free supernatant was tested for the presence of RT activity as a measure of successful infection. The results, shown in FIG. 2, demonstrate that DP-178 (SEQ ID:1) inhibited the de novo infection process mediated by the HIV-1 viral isolate at concentrations as low as 90ng/ml (IC50=90ng/ml). In contrast, the two positive control peptides, DP-125 (SEQ: ID:8) and DP-118 (SEQ ID:10), had over 60-fold higher IC50 concentrations of approximately 5 μ g/ml.

In a separate experiment, the HIV-1 and HIV-2 inhibitory action of DP-178 (SEQ ID:1) was tested with CEM cells and either HIV-1_{LAI} or HIV-2_{NIHZ}. 62 TCID₅₀

HIV-1_{LAI} or 25 GCID₅₀ HIV-2_{NIHZ} were used in these experiments, and were incubated for 7 days. As may be seen in FIG. 3, DP-178 (SEQ ID:1) inhibited HIV-1 infection with an IC₅₀ of about 31ng/ml. In contrast, DP-178 (SEQ ID:1) exhibited a much higher IC₅₀ for 5 HIV-2_{NIHZ}, thus making DP-178 (SEQ ID:1) two logs more potent as a HIV-1 inhibitor than a HIV-2 inhibitor. This finding is consistent with the results of the 10 fusion inhibition assays described, above, in Section 6.2.1, and further supports a significant level of 15 selectivity (i.e., for HIV-1 over HIV-2).

7. EXAMPLE: THE HIV-1 INHIBITOR, DP-178 (SEQ ID:1) IS NON-CYTOXIC

In this Example, the 36 amino acid synthetic 15 peptide inhibitor DP-178 (SEQ ID:1) is shown to be non-cytotoxic to cells in culture, even at the highest peptide concentrations (40 μ g/ml) tested.

7.1. MATERIALS AND METHODS

20 Cell proliferation and toxicity assay: Approximately 3.8x10⁵ CEM cells for each peptide concentration were incubated for 3 days at 37°C in T25 flasks. Peptides tested were DP-178 (SEQ ID:1) and DP-116 (SEQ ID:9), as described in FIG. 1. The 25 concentrations of each peptide used were 0, 2.5, 10, and 40 μ g/ml. Cell counts were taken at incubation times of 0, 24, 48, and 72 hours.

7.2. RESULTS

30 Whether the potent HIV-1 inhibitor DP-178 (SEQ ID:1) exhibited any cytotoxic effects was assessed by assaying the peptide's effects on the proliferation and viability of cells in culture. CEM cells were incubated in the presence of varying concentrations of 35 DP-178 (SEQ ID:1), and DP-116 (SEQ ID:9), a peptide

previously shown to be ineffective as a HIV inhibitor (Wild, C. *et al.*, 1992, Proc. Natl. Acad. Sci. USA **89**:10,537-10,541). Additionally, cells were incubated in the absence of either peptide.

The results of the cytotoxicity study demonstrate 5 that DP-178 (SEQ ID:1) exhibits no cytotoxic effects on cells in culture. As can be seen, below, in Table XI, even the proliferation and viability characteristics of cells cultured for 3 days in the presence of the highest concentration of DP-178 (SEQ 10 ID:1) tested (40 μ g/ml) do not significantly differ from the DP-116 (SEQ ID:9) or the no-peptide controls. The cell proliferation data is also represented in graphic form in FIG. 6. As was demonstrated in the 15 Working Example presented above in Section 6, DP-178 (SEQ ID:1) completely inhibits HIV-1 mediated syncytia formation at peptide concentrations between 1 and 10ng/ml, and completely inhibits cell-free viral infection at concentrations of at least 90ng/ml. Thus, this study demonstrates that even at peptide 20 concentrations greater than 3 log higher than the HIV inhibitory dose, DP-178 (SEQ ID:1) exhibits no cytotoxic effects.

TABLE XI

	<u>Peptide</u>	<u>Concentration</u> μ g/ml	% Viability at time (hours)			
			0	24	48	72
30	DP178 (SEQ ID:1)	40		98	97	95
		10		98	97	98
		2.5		98	93	96

35

DP116 (SEQ ID:9)	40	98	95	98	97
	10	98	95	93	98
	2.5	98	96	98	99
5					
No Peptide	0	98	97	99	98

10 8. EXAMPLE: THE INTERACTION OF DP178 AND DP107

15 Soluble recombinant forms of gp41 used in the example described below provide evidence that the DP178 peptide associates with a distal site on gp41 whose interactive structure is influenced by the DP107 leucine zipper motif. A single mutation disrupting the coiled-coil structure of the leucine zipper domain transformed the soluble recombinant gp41 protein from an inactive to an active inhibitor of HIV-1 fusion. This transformation may result from liberation of the 20 potent DP178 domain from a molecular clasp with the leucine zipper, DP107, determinant. The results also indicate that the anti-HIV activity of various gp41 derivatives (peptides and recombinant proteins) may be due to their ability to form complexes with viral gp41 25 and interfere with its fusogenic process.

8.1. MATERIALS AND METHODS

8.1.1. CONSTRUCTION OF FUSION PROTEINS
AND GP41 MUTANTS

30 Construction of fusion proteins and mutants shown in FIG. 7 was accomplished as follows: the DNA sequence corresponding to the extracellular domain of gp41 (540-686) was cloned into the Xmn I site of the expression vector pMal-p2 (New England Biolab) to give 35 M41. The gp41 sequence was amplified from pgtat

(Malim et al., 1988, *Nature* 355: 181-183) by using polymerase chain reaction (PCR) with upstream primer 5'-ATGACGCTGACGGTACAGGCC-3' (primer A) and downstream primer 5'-TGACTAAGCTTAATACCACAGCCAATTGTTAT-3' (primer B). M41-P was constructed by using the T7-Gen 5 in vitro mutagenesis kit from United States Biochemicals (USB) following the supplier's instructions. The mutagenic primer (5'-GGAGCTGCTGGGGCCCCAGAC-3') introduces an Ile to Pro mutation in M41 at position 578. M41Δ107 was made 10 using a deletion mutagenic primer 5'-CCAAATCCCCAGGAGCTGCTCGAGCTGCACTATACCAGAC-3' (primer C) following the USB T7-Gen mutagenesis protocol. M41Δ178 was made by cloning the DNA fragment corresponding to gp41 amino acids 540-642 into the Xmn 15 I site of pMal-p2. Primer A and 5'-ATAGCTTCTAGATTAATTGTTAATTCTCTGTCCC-3' (primer D) were used in the PCR with the template pgtat to generate the inserted DNA fragments. M41-P was used as the template with primer A and D in PCR to generate M41- 20 PΔ178. All inserted sequences and mutated residues were checked by restriction enzyme analysis and confirmed by DNA sequencing.

25 8.1.2. PURIFICATION AND CHARACTERIZATION OF FUSION PROTEINS

The fusion proteins were purified according to the protocol described in the manufacturer's brochure of protein fusion and purification systems from New England Biolabs (NEB). Fusion proteins (10 ng) were 30 analyzed by electrophoresis on 8% SDS polyacrylamide gels. Western blotting analysis was performed as described by Sambrook et al, 1989, *Molecular Cloning: A Laboratory Manual*, 2d Ed, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, Ch. 18, 35 pp. 64-75. An HIV-1 positive serum diluted 1000-fold,

or a human Fab derived from repertoire cloning was used to react with the fusion proteins. The second antibody was HRP-conjugated goat antihuman Fab. An ECL Western blotting detection system (Amersham) was used to detect the bound antibody. A detailed 5 protocol for this detection system was provided by the manufacturer. Rainbow molecular weight marker (Amersham) were used to estimate the size of fusion proteins.

10 8.1.3. CELL FUSION ASSAYS FOR ANTI-HIV ACTIVITY

Cell fusion assays were performed as previously described (Matthews et al., 1987, Proc. Natl. Acad. Sci. USA 84: 5424-5481). CEM cells (7×10^4) were 15 incubated with HIV-1_{MB} chronically infected CEM cells (10^4) in 96-well flat-bottomed half-area plates (Costar) in 100 μ l culture medium. Peptide and fusion proteins at various concentrations in 10 μ l culture medium were incubated with the cell mixtures at 37°C 20 for 24 hours. Multinucleated syncytia were estimated with microscopic examination. Both M41 and M41-P did not show cytotoxicity at the concentrations tested and shown in FIG. 8.

Inhibition of HIV-1 induced cell-cell fusion activity was carried out in the presence of 10 nM 25 DP178 and various concentrations of M41 Δ 178 or M41-P Δ 178 as indicated in FIG. 9. There was no observable syncytia in the presence of 10 nM DP178. No peptide or fusion protein was added in the control samples.

30 8.1.4. ELISA ANALYSIS OF DP178 BINDING TO THE LEUCINE ZIPPER MOTIF OF GP41

The amino acid sequence of DP178 used is: YTSLIHSILIEESQNLQQEKNEQELLELDKWASLWNWF. For enzyme linked immunoassay (ELISA), M41 Δ 178 or M41-P Δ 178 (5 35 μ g/ml) in 0.1M NaHCO₃, pH 8.6, were coated on 96 wells

Linbro ELISA plates (Flow Lab, Inc.) overnight. Each well was washed three times with distilled water then blocked with 3% bovine serum albumin (BSA) for 2 hours. After blocking, peptides with 0.5% BSA in TBST (40 mM Tris-HCl pH7.5, 150 mM NaCl, 0.05% Tween 20) 5 were added to the ELISA plates and incubated at room temperature for 1 hour. After washing three times with TBST, Fab-d was added at a concentration of 10 ng/ml with 0.5% BSA in TBST. The plates were washed three times with TBST after incubation at room 10 temperature for 1 hour. Horse radish peroxidase (HRP) conjugated goat antihuman Fab antiserum at a 2000 fold dilution in TBST with 0.5% BSA was added to each well and incubated at room temperature for 45 minutes. The plates were then washed four times with TBST. The 15 peroxidase substrate o-phenylene diamine (2.5 mg/ml) and 0.15% H₂O₂ were added to develop the color. The reaction was stopped with an equal volume of 4.5 N H₂SO₄ after incubation at room temperature for 10 minutes. The optical density of the stopped reaction 20 mixture was measured with a micro plate reader (Molecular Design) at 490 nm. Results are shown in FIG. 10.

8.2. RESULTS

8.2.1. THE EXPRESSION AND CHARACTERIZATION OF THE ECTODOMAIN OF GP41

As a step toward understanding the roles of the two helical regions in gp41 structure and function, the ectodomain of gp41 was expressed as a maltose 25 binding fusion protein (M41) (Fig. 7). The fusogenic peptide sequence at the N-terminal of gp41 was omitted from this recombinant protein and its derivatives to improve solubility. The maltose binding protein facilitated purification of the fusion proteins under 30 relatively mild, non-denaturing conditions. Because 35

the M41 soluble recombinant gp41 was not glycosylated, lacked several regions of the transmembrane protein (i.e., the fusion peptide, the membrane spanning, and the cytoplasmic domains), and was expressed in the absence of gp120, it was not expected to precisely reflect the structure of native gp41 on HIV-1 virions. Nevertheless, purified M41 folded in a manner that preserved certain discontinuous epitopes as evidenced by reactivity with human monoclonal antibodies, 98-6, 126-6, and 50-69, previously shown to bind conformational epitopes on native gp41 expressed in eukaryotic cells (Xu et al., 1991, J. Virol. 65: 4832-4838; Chen, 1994, J. Virol. 68:2002-2010). Thus, at least certain regions of native gp41 defined by these antibodies appear to be reproduced in the recombinant fusion protein M41. Furthermore, M41 reacted with a human recombinant Fab (Fab-d) that recognizes a conformational epitope on gp41 and binds HIV-1 virions as well as HIV-1 infected cells but not uninfected cells as analyzed by FACS. Deletion of either helix motif, i.e., DP107 or DP178, of the M41 fusion protein eliminated reactivity with Fab-d. These results indicate that both helical regions, separated by 60 amino acids in the primary sequence, are required to maintain the Fab-d epitope.

25

8.2.2. ANTI-HIV ACTIVITY OF THE RECOMBINANT ECTODOMAIN OF GP41

The wild type M41 fusion protein was tested for anti-HIV-1 activity. As explained, supra, synthetic peptides corresponding to the leucine zipper (DP107) and the C-terminal putative helix (DP178) show potent anti-HIV activity. Despite inclusion of both these regions, the recombinant M41 protein did not affect

35

HIV-1 induced membrane fusion at concentrations as high as 50 μ M (Table XII, below).

5 **TABLE XII**
DISRUPTION OF THE LEUCINE ZIPPER OF
GP41 FREES THE ANTI-HIV MOTIF

		<u>DP107</u>	<u>DP178</u>	<u>M41</u>	<u>M41-P</u>	<u>M41-PΔ178</u>
	Cell fusion (IC ₅₀)	1 μ M	1 nM	> 50 μ M	83 nM	> 50 μ M
10	Fab-D binding (k _D)	-	-	3.5x10 ⁻⁹	2.5x10 ⁻⁸	-
	HIV infectiv- ity (IC ₅₀)	1 μ M	80 nM	> 16 μ M	66 nM	> 8 μ M

15

1 The affinity constants of Fab-d binding to the fusion proteins were determined using a protocol described by B. Friguet et al., 1985, J. Immunol. Method. 77:305-319.

20

- = No detectable binding of Fab-d to the fusion proteins.

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Antiviral Infectivity Assays. 20 μ l of serially diluted virus stock was incubated for 60 minutes at ambient temperature with 20 μ l of the indicated concentration of purified recombinant fusion protein in RPMI 1640 containing 10% fetal bovine serum and antibiotics in a 96-well microtiter plate. 20 μ l of CEM4 cells at 6 x 10⁵ cells/ml were added to each well, and cultures were incubated at 37°C in a humidified CO₂ incubator. Cells were cultured for 9 days by the addition of fresh medium every 2 to 30 days. On days 5, 7, and 9 postinfection, supernatant samples were assayed for reverse transcriptase (RT) activity, as described below, to monitor viral replication. The 50% tissue culture infectious dose (TCID₅₀) was calculated for each condition according to the formula of Reed & Muench, 1937, Am. J. Hyg. 27:493-497. RT activity was determined by a modification of the published methods of Goff et al., 1981, J. Virol. 38:239-248 and Willey et al., 1988, J. Virol. 62:139-147 as described in Chen et al., 1993, AIDS Res. Human Retroviruses 9:1079-1086.

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35 Surprisingly, a single amino acid substitution, proline in place of isoleucine in the middle of the leucine zipper motif, yielded a fusion protein (M41-P)

which did exhibit antiviral activity (Table XII and Fig. 8). As seen in Table XII, M41-P blocked syncytia formation by 90% at approximately 85 nM and neutralized HIV-1_{WB} infection by 90% at approximately 70 nM concentrations. The anti-HIV-1 activity of M41-
5 P appeared to be mediated by the C-terminal helical sequence since deletion of that region from M41-P yielded an inactive fusion protein, M41-PΔ178 (Table XII). That interpretation was reinforced by experiments demonstrating that a truncated fusion
10 protein lacking the DP178 sequence, M41Δ178, abrogated the potent anti-fusion activity of the DP178 peptide in a concentration-dependent manner (FIG. 9). The same truncated fusion protein containing the proline mutation disrupting the leucine zipper, M41-PΔ178, was
15 not active in similar competition experiments (FIG. 9). The results indicate that the DP178 peptide associates with a second site on gp41 whose interactive structure is dependent on a wild type leucine zipper sequence. A similar interaction may
20 occur within the wild type fusion protein, M41, and act to form an intramolecular clasp which sequesters the DP178 region, making it unavailable for anti-viral activity.

A specific association between these two domains
25 is also indicated by other human monoclonal Fab-d studies. For example, Fab-d failed to bind either the DP178 peptide or the fusion protein M41Δ178, but its epitope was reconstituted by simply mixing these two reagents together (FIG. 10). Again, the proline
30 mutation in the leucine zipper domain of the fusion protein, M41-PΔ178, failed to reconstitute the epitope in similar mixing experiments.

9. EXAMPLE: METHOD FOR COMPUTER-ASSISTED
IDENTIFICATION OF DP-107-LIKE
AND DP-178-LIKE SEQUENCES

A number of known coiled-coil sequences have been well described in the literature and contain heptad repeat positioning for each amino acid. Coiled-coil nomenclature labels each of seven amino acids of a heptad repeat A through G, with amino acids A and D tending to be hydrophobic positions. Amino acids E and G tend to be charged. These four positions (A, D, E, and G) form the amphipathic backbone structure of a monomeric alpha-helix. The backbones of two or more amphipathic helices interact with each other to form di-, tri-, tetrameric, etc., coiled-coil structures.

In order to begin to design computer search motifs, a series of well characterized coiled coils were chosen including yeast transcription factor GCN4, Influenza Virus hemagglutinin loop 36, and human proto-oncogenes c-Myc, c-Fos, and c-Jun. For each peptide sequence, a strict homology for the A and D positions, and a list of the amino acids which could be excluded for the B, C, E, F, and G positions (because they are not observed in these positions) was determined. Motifs were tailored to the DP-107 and DP-178 sequences by deducing the most likely possibilities for heptad positioning of the amino acids of HIV-1 Bru DP-107, which is known to have coiled-coil structure, and HIV-1 Bru DP-178, which is still structurally undefined. The analysis of each of the sequences is contained in FIG. 12. For example, the motif for GCN4 was designed as follows:

1. The only amino acids (using standard single letter amino acid codes) found in the A or D positions of GCN4 were [LMNV].
2. All amino acids were found at B, C, E, F, and G positions except {CFGIMPTW}.

3. The PESEARCH motif would, therefore, be written as follows:

[LMNV]-{CFGIMPTW} (2)-[LMNV]-{CFGIMPTW} (3)-

[LMNV]-{CFGIMPTW} (2)-[LMNV]-{CFGIMPTW} (3)-

[LMNV]-{CFGIMPTW} (2)-[LMNV]-{CFGIMPTW} (3)-

5 [LMNV]-{CFGIMPTW} (2)-[LMNV]-{CFGIMPTW} (3)

Translating or reading the motif: "at the first A position either L, M, N, or V must occur; at positions B and C (the next two positions) accept everything 10 except C, F, G, I, M, P, T, or W; at the D position either L, M, N, or V must occur; at positions E, F, and G (the next 3 positions) accept everything except C, F, G, I, M, P, T, or W." This statement is contained four times in a 28-mer motif and five times 15 in a 35-mer motif. The basic motif key then would be: [LMNV]-{CFGIMPTW}. The motif keys for the remaining well described coiled-coil sequences are summarized in FIG. 12.

20 The motif design for DP-107 and DP-178 was slightly different than the 28-mer model sequences described above due to the fact that heptad repeat positions are not defined and the peptides are both longer than 28 residues. FIG. 13 illustrates several 25 possible sequence alignments for both DP-107 and DP-178 and also includes motif designs based on 28-^{mer}, 35-^{mer}, and full-length peptides. Notice that only slight differences occur in the motifs as the peptides are lengthened. Generally, lengthening the base 30 peptide results in a less stringent motif. This is very useful in broadening the possibilities for identifying DP-107- or DP-178-like primary amino acid sequences referred to in this document as "hits".

35 In addition to making highly specific motifs for each type peptide sequence to be searched, it is also possible to make "hybrid" motifs. These motifs are

made by "crossing" two or more very stringent motifs to make a new search algorithm which will find not only both "parent" motif sequences but also any peptide sequences which have similarities to one, the other, or both "parents". For example, in Table 3 the 5 "parent" sequence of GCN4 is crossed with each of the possible "parent" motifs of DP-107. Now the hybrid motif must contain all of the amino acids found in the A and D positions of both parents, and exclude all of the amino acids not found in either parent at the 10 other positions. The resulting hybrid from crossing GCN4 or [LMNV]{CFGIMPTW} and DP-107 (28-mer with the first L in the D position) or [ILQQT]{CDFIMPST}, is [ILMNQTV]{CFIMPT}. Notice that now only two basic 15 hybrid motifs exist which cover both framing possibilities, as well as all peptide lengths of the parent DP-107 molecule. FIG. 15 represents the hybridizations of GCN4 with DP-178. FIG. 16 represents the hybridizations of DP-107 and DP-178. It is important to keep in mind that the represented 20 motifs, both parent and hybrid, are motif keys and not the depiction of the full-length motif needed to actually do the computer search.

Hybridizations can be performed on any 25 combination of two or more motifs. Table 5 summarizes several three-motif hybridizations including GCN4, DP-107 (both frames), and DP-178 (also both frames). Notice that the resulting motifs are now becoming much more similar to each other. In fact, the first and third hybrid motifs are actually 30 subsets of the second and fourth hybrid motifs respectively. This means that the first and third hybrid motifs are slightly more stringent than the second and fourth. It should also be noted that with only minor changes in these four motifs, or by 35 hybridizing them, a single motif could be obtained

which would find all of the sequences. However, it should be remembered that stringency is also reduced. Finally, the most broad-spectra and least-stringent hybrid motif is described in FIG. 18 which summarizes the hybridization of GCN4, DP-107 (both frames), DP-178 (both frames), c-Fos, c-Jun, c-Myc, and Flu loop 36.

A special set of motifs was designed based on the fact that DP-178 is located only approximately ten amino acids upstream of the transmembrane spanning region of gp41 and just C-terminal to a proline which separates DP-107 and DP-178. It has postulated that DP-178 may be an amphipathic helix when membrane associated, and that the proline might aid in the initiation of the helix formation. The same arrangement was observed in Respiratory Syncytial Virus; however, the DP-178-like region in this virus also had a leucine zipper just C-terminal to the proline. Therefore, designed N-terminal proline-leucine zipper motifs were designed to analyze whether any other viruses might contain this same pattern. The motifs are summarized in FIG. 19.

The PC/Gene protein database contains 5879 viral amino acid sequences (library file PVIRUSES; CD-ROM release 11.0). Of these, 1092 are viral envelope or glycoprotein sequences (library file PVIRUSE1). Tables V through X contain lists of protein sequence names and motif hit locations for all the motifs searched.

**30 10. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION
OF DP-107 AND DP-178-LIKE SEQUENCES
IN HUMAN IMMUNODEFICIENCY VIRUS**

FIG. 20 represents search results for HIV-1 BRU isolate gp41 (PC/Gene protein sequence PENV_HV1BR).
35 Notice that the hybrid motif which crosses DP-107 and

DP-178 (named 107x178x4; the same motif as found in FIG. 16 found three hits including amino acids 550-599, 636-688, and 796-823. These areas include DP-107 plus eight N-terminal and four C-terminal amino acids; DP-178 plus seven N-terminal and ten C-terminal amino acids; and an area inside the transmembrane region (cytoplasmic). FIG. 20 also contains the results obtained from searching with the motif named ALLMOTI5, for which the key is found in FIG. 17 ({CDGHP}{CFP}x5). This motif also found three hits including DP-107 (amino acids 510-599), DP-178 (615-717), and a cytoplasmic region (772-841). These hits overlap the hits found by the motif 107x178x4 with considerable additional sequences on both the amino and carboxy termini. This is not surprising in that 107x178x4 is a subset of the ALLMOTI5 hybrid motif. Importantly, even though the stringency of ALLMOTI5 is considerably less than 107x178x4, it still selectively identifies the DP-107 and DP-178 regions of gp41 shown to contain sequences for inhibitory peptides of HIV-1. The results of these two motif searches are summarized in Table V under the PC/Gene protein sequence name PENV HV1BR. The proline-leucine zipper motifs also gave several hits in HIV-1 BRU including 503-525 which is at the very C-terminus of gp120, just upstream of the cleavage site (P7LZIPC and P12LZIPC); and 735-768 in the cytoplasmic domain of gp41 (P23LZIPC). These results are found in Tables VIII, IX, and X under the same sequence name as mentioned above. Notice that the only area of HIV-1 BRU which is predicted by the Lupas algorithm to contain a coiled-coil region, is from amino acids 635-670. This begins eight amino acids N-terminal to the start and ends eight amino acids N-terminal to the end of DP-178. DP-107, despite the fact that it is a known coiled coil, is

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not predicted to contain a coiled-coil region using the Lupas method.

11. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION
5 OF DP-107-LIKE AND DP-178-LIKE
SEQUENCES IN HUMAN RESPIRATORY
SYNCYTIAL VIRUS

FIG. 21 represents search results for Human Respiratory Syncytial Virus (RSV; Strain A2) fusion glycoprotein F1 (PC/Gene protein sequence name PVGLF_HRSVA). Motif 107x178x4 finds three hits including amino acids 152-202, 213-243, and 488-515. The arrangement of these hits is similar to what is found in HIV-1 except that the motif finds two regions with similarities to DP-178, one just downstream of what would be called the DP-107 region or amino acids 213-243, and one just upstream of the transmembrane region (also similar to DP-178) or amino acids 488-515. Motif ALLMOTI5 also finds three areas including amino acids 116-202, 267-302, and 506-549. The proline-leucine zipper motifs also gave several hits including amino acids 205-221 and 265-287 (P1LZIPC 265-280, P12LZIPC), and 484-513 (P7LZIPC and P12LZIPC 484-506, P23LZIPC). Notice that the PLZIP motifs also identify regions which share location similarities with DP-178 of HIV-1.

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12. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF
DP-107-LIKE AND DP-178-LIKE SEQUENCES
IN SIMIAN IMMUNODEFICIENCY VIRUS

Motif hits for Simian immunodeficiency Virus gp41
30 (AGM3 isolate; PC/Gene protein sequence name PENV_SIVAG) are shown in FIG. 22. Motif 107x178x4 finds three hits including amino acids 566-593, 597-624, and 703-730. The first two hits only have three amino acids between them and could probably be
35 combined into one hit from 566-624 which would

represent a DP-107-like hit. Amino acids 703 to 730 would then represent a DP-178-like hit. ALLMOTI5 also finds three hits including amino acids 556-628 (DP-107-like), 651-699 (DP-178-like), and 808-852 which represents the transmembrane spanning region. SIV

5 also has one region from 655-692 with a high propensity to form a coiled coil as predicted by the Lupas algorithm. Both 107x178x4 and ALLMOTI5 motifs find the same region. SIV does not have any PLZIP motif hits in gp41.

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13. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF
DP-107-LIKE AND DP-178 LIKE SEQUENCES
IN CANINE DISTEMPER VIRUS

Canine Distemper Virus (strain Onderstepoort)

15 fusion glycoprotein F1 (PC/Gene Protein sequence name PVGLF_CDVO) has regions similar to Human RSV which are predicted to be DP-107-like and DP-178-like (FIG. 23). Motif 107x178x4 highlights one area just C-terminal to the fusion peptide at amino acids 252-293. Amino acids 252-286 are also predicted to be coiled coil using the Lupas algorithm. Almost 100 amino acids C-terminal to the first region is a DP-178-like area at residues 340-367. ALLMOTI5 highlights three areas of interest including: amino acids 228-297, which 20 completely overlaps both the Lupas prediction and the DP-107-like 107x178x4 hit; residues 340-381, which overlaps the second 107x178x4 hit; and amino acids 568-602, which is DP178-like in that it is located just N-terminal to the transmembrane region. It also 25 overlaps another region (residues 570-602) predicted by the Lupas method to have a high propensity to form a coiled coil. Several PLZIP motifs successfully identified areas of interest including P6 and P12LZIPC which highlight residues 336-357 and 336-361 30 35 respectively; P1 and P12LZIPC which find residues 398-

414; and P12 and P23LZIPC which find residues 562-589 and 562-592 respectively.

14. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF
DP-107-LIKE AND DP-178-LIKE SEQUENCES
IN NEWCASTLE DISEASE VIRUS

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FIG. 24 shows the motif hits found in Newcastle Disease Virus (strain Australia-Victoria/32; PC Gene protein sequence name PVGLF_NDVA). Motif 107x178x4 finds two areas including a DP-107-like hit at amino acids 151-178 and a DP-178-like hit at residues 426-512. ALLMOTI5 finds three areas including residues 117-182, 231-272, and 426-512. The hits from 426-512 include a region which is predicted by the Lupas method to have a high coiled-coil propensity (460-503). The PLZIP motifs identify only one region of interest at amino acids 273-289 (P1 and 12LZIPC).

15. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION
OF DP-107-LIKE AND DP-178-LIKE
SEQUENCES IN HUMAN PARAINFLUENZA VIRUS

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Both motifs 107x178x4 and ALLMOTI5 exhibit DP-107-like hits in the same region, 115-182 and 117-182 respectively, of Human Parainfluenza Virus (strain NIH 47885; PC/Gene protein sequence name PVGLF_p13H4; (FIG. 25). In addition, the two motifs have a DP-178-like hit just slightly C-terminal at amino acids 207-241. Both motifs also have DP-178-like hits nearer the transmembrane region including amino acids 457-497 and 462-512 respectively. Several PLZIP motif hits are also observed including 283-303 (P5LZIPC), 283-310 (P12LZIPC), 453-474 (P6LZIPC), and 453-481 (P23LZIPC). The Lupas algorithm predicts that amino acids 122-176 have a propensity to form a coiled-coil.

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16. EXAMPLE: COMPUTER-ASSISTED IDENTIFICATION OF
DP-107-LIKE AND DP-178-LIKE SEQUENCES OF
INFLUENZA A VIRUS

FIG. 26 illustrates the Lupas prediction for a coiled coil in Influenza A Virus (strain A/Aichi/2/68) at residues 379-436, as well as the motif hits for 107x178x4 at amino acids 387-453, and for ALLMOTI5 at residues 380-456. Residues 383-471 (38-125 of HA2) were shown by Carr and Kim to be an extended coiled coil when under acidic pH (Carr and Kim, 1993, Cell 10 73: 823-832). The Lupas algorithyan predicts a coiled-coil at residues 379-436. All three methods successfully predicted the region shown to actually have coiled-coil structure; however, ALLMOTI5 predicted the greatest portion of the 88 residue 15 stretch.

17. EXAMPLE: RSV ANTIVIRAL COMPOUNDS

In the Example presented herein, respiratory syncytial virus (RSV) peptide sequences identified by 20 utilizing the computer-assisted coiled-coil peptide sequence searches described in Example 9, above, are shown to encode peptide domains that exhibit structural similarity to actual, known coiled-coil peptides, and are, additionally found to exhibit 25 antiviral activity.

17.1 MATERIALS AND METHODS

Structural analyses consisted of circular dichroism (CD) studies, which were conducted according 30 to the methods described in the Applicants' co-pending U.S. Patent Application Ser. No 08/073,028.

Anti-RSV antiviral activity was assayed as described in Pringle, C.R. et al., 1985, J. Medical Vir. 17:377-386.

A 48 amino acid RSV F2 peptide and a 53 amino acid RSV T67 peptide are utilized which span sequences that were identified via the computer assisted peptide sequence search strategies described in Example 9, above. See FIG. 21 for the exact position of these 5 sequences and for the motifs utilized.

17.2 RESULTS

35-mer oligopeptides were synthesized which constituted portions of the 48 amino acid RSV F2 peptide sequence (FIG. 27) and portions of the 53 amino acid RSV T67 peptide sequence (FIG. 28). The 10 oligopeptides were assayed, via CD analysis, for structural similarity to known coiled-coil structures, and for anti-RSV activity. As shown in FIGS. 27 and 15 28, a number of these oligopeptides exhibited substantial coiled-coil structural similarity and/or antiviral activity.

Thus, the computer assisted searches described, herein, in Example 9, for example, successfully 20 identified viral peptide domains that represent highly promising anti-RSV antiviral compounds.

18. EXAMPLE: HPF3 ANTIVIRAL COMPOUNDS

In the Example presented herein, human 25 parainfluenza virus 3 (HPF3) peptide sequences identified by utilizing the computer-assisted coiled-coil peptide sequence searches described in Example 9, above, are shown to encode peptide domains that 30 exhibit structural similarity to actual, known coiled-coil peptides, and are, additionally found to exhibit antiviral activity.

18.1 MATERIALS AND METHODS

Structural analyses consisted of circular 35 dichroism (CD) studies, which were conducted according

to the methods described in the Applicants' co-pending U.S. Patent Application Ser. No 08/073,028.

Anti-HPF3 antiviral activity was assayed as described in Pringle, C.R. et al., 1985, J. Medical Vir. 17:377-386.

5 A 56 amino acid and 70 amino acid HPF3 peptide are utilized which span sequences that were identified via the computer assisted peptide sequence search strategies described in Example 9, above. See FIG. 25 for the exact positions of these sequences and for the
10 motifs utilized.

18.2 RESULTS

35-mer oligopeptides were synthesized which constituted portions of the 56 amino acid HPF3 peptide sequence (FIG. 29) and portions of the 70 amino acid HPF3 peptide sequence (FIG. 30). The oligopeptides were assayed, via CD analysis, for structural similarity to known coiled-coil structures, and for anti-HPF3 activity. As shown in FIGS. 29 and 30, a
20 number of these oligopeptides exhibited substantial coiled-coil structural similarity and/or antiviral activity.

25 Thus, the computer assisted searches described, herein, in Example 9, for example, successfully identified viral peptide domains that represent highly promising anti-HPF3 antiviral compounds.

30 The present invention is not to be limited in scope by the specific embodiments described which are intended as single illustrations of individual aspects of the invention, and functionally equivalent methods and components are within the scope of the invention. Indeed, various modifications of the invention, in addition to those shown and described herein will
35 become apparent to those skilled in the art from the

foregoing description and accompanying drawings. Such modifications are intended to fall within the scope of the appended claims.

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WHAT IS CLAIMED IS:

1. A peptide having an amino acid sequence corresponding to an α -helix region of an extracellular domain of a viral envelope protein, which interacts
5 with and binds to a second α -helix region of the viral envelope protein containing a leucine-zipper domain having a coiled-coil structure.
2. The peptide of Claim 1 wherein the peptide
10 is recognized by a computer-assisted peptide sequence search utilizing an ALLMOT15, 107x178x4 motif, or a PLZIP motif.
3. The peptide of Claim 1 in which the
15 enveloped virus is a retrovirus.
4. The peptide of Claim 3 in which the retrovirus is a human retrovirus.
- 20 5. The peptide of Claim 4 in which the human retrovirus is HIV-1 or HIV-2.
6. The peptide of Claim 4 in which the human retrovirus is HTLV-I or HTLV-II
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7. The peptide of Claim 1 in which the enveloped virus is a non-human retrovirus.
8. The peptide of Claim 6 in which the non-
30 human retrovirus is bovine leukosis virus, feline sarcoma virus, feline leukemia virus, simian immunodeficiency virus, simian sarcoma virus, and sheep progress pneumonia virus.

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9. The peptide of Claim 1 in which the enveloped virus is a non-retroviral virus.

10. The peptide of Claim 9 in which the virus is respiratory syncytial virus, influenza virus,
5 parainfluenza virus, canine distemper virus, or newcastle disease virus.

11. A peptide having a formula selected from the group consisting of:

10 X-YTS-Z
X-YTSL-Z
X-YTSLI-Z
X-YTSLIH-Z
X-YTSLIHS-Z
X-YTSLIHSL-Z
X-YTSLIHSЛИ-Z
15 X-YTSLIHSЛИE-Z
X-YTSLIHSЛИEE-Z
X-YTSLIHSЛИEES-Z
X-YTSLIHSЛИEESQ-Z
X-YTSLIHSЛИEESQN-Z
X-YTSLIHSЛИEESQNQQ-Z
20 X-YTSLIHSЛИEESQNQQE-Z
X-YTSLIHSЛИEESQNQQEK-Z
X-YTSLIHSЛИEESQNQQEKN-Z
X-YTSLIHSЛИEESQNQQEKNE-Z
X-YTSLIHSЛИEESQNQQEKNEQ-Z
X-YTSLIHSЛИEESQNQQEKNEQE-Z
25 X-YTSLIHSЛИEESQNQQEKNEQEL-Z
X-YTSLIHSЛИEESQNQQEKNEQELL-Z
X-YTSLIHSЛИEESQNQQEKNEQELLE-Z
X-YTSLIHSЛИEESQNQQEKNEQELLED-Z
X-YTSLIHSЛИEESQNQQEKNEQELLELDK-Z
X-YTSLIHSЛИEESQNQQEKNEQELLELDKWA-Z
X-YTSLIHSЛИEESQNQQEKNEQELLELDKWAS-Z
30 X-YTSLIHSЛИEESQNQQEKNEQELLELDKWASL-Z
X-YTSLIHSЛИEESQNQQEKNEQELLELDKWASLW-Z
X-YTSLIHSЛИEESQNQQEKNEQELLELDKWASLWN-Z
X-YTSLIHSЛИEESQNQQEKNEQELLELDKWASLWNW-Z and
X-YTSLIHSЛИEESQNQQEKNEQELLELDKWASLWNWF-Z (SEQ ID:1), or

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X-NWF-Z
 X-WNWF-Z
 X-LWNWF-Z
 X-SLWNWF-Z
 X-ASLWNWF-Z
 X-WASLWNWF-Z
 X-KWASLWNWF-Z
 X-DKWASLWNWF-Z
 X-LDKWASLWNWF-Z
 X-ELDKWASLWNWF-Z
 X-LLELDKWASLWNWF-Z
 X-ELLELDKWASLWNWF-Z
 X-QELLELDKWASLWNWF-Z
 X-EQELLELDKWASLWNWF-Z
 X-NEQELLELDKWASLWNWF-Z
 X-KNEQELLELDKWASLWNWF-Z
 X-EKNEQELLELDKWASLWNWF-Z
 X-QEKNEQELLELDKWASLWNWF-Z
 X-QQEKNEQELLELDKWASLWNWF-Z
 X-NQQEKNEQELLELDKWASLWNWF-Z
 X-QNQQEKNEQELLELDKWASLWNWF-Z
 X-SQNQQEKNEQELLELDKWASLWNWF-Z
 X-ESQNQQEKNEQELLELDKWASLWNWF-Z
 X-EESQNQQEKNEQELLELDKWASLWNWF-Z
 X-LIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-SLIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-HSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-IHSLIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-LIHSILIEESQNQQEKNEQELLELDKWASLWNWF-Z
 X-SLIHSILIEESQNQQEKNEQELLELDKWASLWNWF-Z
 and X-TSLIHSILIEESQNQQEKNEQELLELDKWASLWNWF-Z

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in which:

25 amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluorenylmethoxy-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

30 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

35 12. A peptide having a formula selected from the group consisting of:

X-LEA-Z
 X-LEAN-Z
 X-LEANI-Z
 X-LEANIS-Z
 X-LEANISQ-Z
 X-LEANISQS-Z
 X-LEANISQSL-Z
 5 X-LEANISQSLE-Z
 X-LEANISQSLEQ-Z
 X-LEANISQSLEQA-Z
 X-LEANISQSLEQAQ-Z
 X-LEANISQSLEQAQI-Z
 X-LEANISQSLEQAQIQ-Z
 X-LEANISQSLEQAQIQQ-Z
 10 X-LEANISQSLEQAQIQQE-Z
 X-LEANISQSLEQAQIQQEKN-Z
 X-LEANISQSLEQAQIQQEKNM-Z
 X-LEANISQSLEQAQIQQEKNMY-Z
 X-LEANISQSLEQAQIQQEKNMYE-Z
 X-LEANISQSLEQAQIQQEKNMYEL-Z
 X-LEANISQSLEQAQIQQEKNMYELQ-Z
 15 X-LEANISQSLEQAQIQQEKNMYELQK-Z
 X-LEANISQSLEQAQIQQEKNMYELQL-Z
 X-LEANISQSLEQAQIQQEKNMYELQKL-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLNS-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLNSW-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLNSWD-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLNSWDV-Z
 20 X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVF-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFT-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTN-Z
 X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNW-Z and
 X-LEANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z (SEQ ID:7), or

X-NWL-Z
 X-TNWL-Z
 X-FTNWL-Z
 X-VFTNWL-Z
 X-DVFTNWL-Z
 X-WDVFTNWL-Z
 X-SWDVFTNWL-Z
 X-NSWDVFTNWL-Z
 X-LNSWDVFTNWL-Z
 X-KLNSWDVFTNWL-Z
 X-QKLNSWDVFTNWL-Z
 X-LQKLNSWDVFTNWL-Z
 X-ELQKLNSWDVFTNWL-Z
 X-YELQKLNSWDVFTNWL-Z
 X-MYELQKLNSWDVFTNWL-Z
 X-NMYELQKLNSWDVFTNWL-Z
 X-KNMYELQKLNSWDVFTNWL-Z
 X-EKNMYELQKLNSWDVFTNWL-Z
 X-QEKNMYELQKLNSWDVFTNWL-Z

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X-QQEKNMYELQKLNSWDVFTNWL-Z
 X-IQQEKNMYELQKLNSWDVFTNWL-Z
 X-QIQQEKNMYELQKLNSWDVFTNWL-Z
 X-AQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-QAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-EQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-LEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-SLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-QKSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-SQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-ISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-NISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 X-ANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z
 and X-EANISQSLEQAQIQQEKNMYELQKLNSWDVFTNWL-Z

10

in which:

amino acid residues are presented by the single-letter code;

15 X comprises an amino group, an acetyl group, a 9-fluoromethyoxyethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

20 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

13. A peptide having a formula selected from the group consisting of:

X-YTS-Z
 X-YTSV-Z
 25 X-YTSVI-Z
 X-YTSVIT-Z
 X-YTSVITI-Z
 X-YTSVITIE-Z
 X-YTSVITIEL-Z
 X-YTSVITIELS-Z
 X-YTSVITIELSN-Z
 30 X-YTSVITIELSNI-Z
 X-YTSVITIELSNIK-Z
 X-YTSVITIELSNIKE-Z
 X-YTSVITIELSNIKEN-Z
 X-YTSVITIELSNIKENK-Z
 X-YTSVITIELSNIKENKC-Z
 X-YTSVITIELSNIKENKCN-Z
 X-YTSVITIELSNIKENKCNG-Z
 35 X-YTSVITIELSNIKENKCGT-Z
 X-YTSVITIELSNIKENKCGTD-Z

X-YTSVITIELSNIKENCNGTDA-Z
 X-YTSVITIELSNIKENCNGTDAK-Z
 X-YTSVITIELSNIKENCNGTDAKV-Z
 X-YTSVITIELSNIKENCNGTDAKVK-Z
 X-YTSVITIELSNIKENCNGTDAVKL-Z
 X-YTSVITIELSNIKENCNGTDAVKLI-Z
 X-YTSVITIELSNIKENCNGTDAVKLIK-Z
5 X-YTSVITIELSNIKENCNGTDAVKLIKQ-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQE-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQEL-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELD-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDK-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKY-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYK-Z
10 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKN-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNA-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAV-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVT-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTE-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTEL-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQ-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQL-Z
15 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLL-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLLM-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLLMQ-Z
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLLMQS-Z and
 X-YTSVITIELSNIKENCNGTDAVKLIKQELDKYKNAVTELQLLMQST-Z, or

X-QST-Z
 X-MQST-Z
 X-LMQST-Z
 X-LLMQST-Z
 X-QLLMQST-Z
 X-LQLLMQST-Z
 X-ELQLLMQST-Z
 X-TELQLLMQST-Z
 X-VTELQLLMQST-Z
20 X-AVTELQLLMQST-Z
 X-NAVTELQLLMQST-Z
 X-KNAVTELQLLMQST-Z
 X-YKNAVTELQLLMQST-Z
 X-KYKNAVTELQLLMQST-Z
 X-DKYKNAVTELQLLMQST-Z
 X-LDKYKNAVTELQLLMQST-Z
 X-ELDKYKNAVTELQLLMQST-Z
 X-QELDKYKNAVTELQLLMQST-Z
 X-KQELDKYKNAVTELQLLMQST-Z
 X-IKQELDKYKNAVTELQLLMQST-Z
 X-LIKQELDKYKNAVTELQLLMQST-Z
 X-KLIKQELDKYKNAVTELQLLMQST-Z
 X-VKLIKQELDKYKNAVTELQLLMQST-Z
 X-KVKLIKQELDKYKNAVTELQLLMQST-Z
25 X-AKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-DAKVKLIKQELDKYKNAVTELQLLMQST-Z

X-QST-Z
 X-MQST-Z
 X-LMQST-Z
 X-LLMQST-Z
 X-QLLMQST-Z
 X-LQLLMQST-Z
 X-ELQLLMQST-Z
 X-TELQLLMQST-Z
 X-VTELQLLMQST-Z
 X-AVTELQLLMQST-Z
 X-NAVTELQLLMQST-Z
 X-KNAVTELQLLMQST-Z
 X-YKNAVTELQLLMQST-Z
 X-KYKNAVTELQLLMQST-Z
 X-DKYKNAVTELQLLMQST-Z
 X-LDKYKNAVTELQLLMQST-Z
 X-ELDKYKNAVTELQLLMQST-Z
 X-QELDKYKNAVTELQLLMQST-Z
 X-KQELDKYKNAVTELQLLMQST-Z
 X-IKQELDKYKNAVTELQLLMQST-Z
 X-LIKQELDKYKNAVTELQLLMQST-Z
 X-KLIKQELDKYKNAVTELQLLMQST-Z
 X-VKLIKQELDKYKNAVTELQLLMQST-Z
 X-KVKLIKQELDKYKNAVTELQLLMQST-Z
30 X-AKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-DAKVKLIKQELDKYKNAVTELQLLMQST-Z

X-QST-Z
 X-MQST-Z
 X-LMQST-Z
 X-LLMQST-Z
 X-QLLMQST-Z
 X-LQLLMQST-Z
 X-ELQLLMQST-Z
 X-TELQLLMQST-Z
 X-VTELQLLMQST-Z
 X-AVTELQLLMQST-Z
 X-NAVTELQLLMQST-Z
 X-KNAVTELQLLMQST-Z
 X-YKNAVTELQLLMQST-Z
 X-KYKNAVTELQLLMQST-Z
 X-DKYKNAVTELQLLMQST-Z
 X-LDKYKNAVTELQLLMQST-Z
 X-ELDKYKNAVTELQLLMQST-Z
 X-QELDKYKNAVTELQLLMQST-Z
 X-KQELDKYKNAVTELQLLMQST-Z
 X-IKQELDKYKNAVTELQLLMQST-Z
 X-LIKQELDKYKNAVTELQLLMQST-Z
 X-KLIKQELDKYKNAVTELQLLMQST-Z
 X-VKLIKQELDKYKNAVTELQLLMQST-Z
 X-KVKLIKQELDKYKNAVTELQLLMQST-Z
35 X-AKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-DAKVKLIKQELDKYKNAVTELQLLMQST-Z

X-TDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-GTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-NGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-CNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-KCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-NKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-ENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 5 X-KENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-IKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-NIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-SNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-LSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-ELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-IELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 10 X-TIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-ITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-VITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-SVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z
 X-TSVITIELSNIKENKCNGTDAKVKLIKQELDKYKNAVTELQLLMQST-Z

in which:

15 amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluoromethoxyethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

20 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

25 14. A peptide having a formula selected from the group consisting of:

X-FYD-Z
 X-FYDP-Z
 X-FYDPL-Z
 X-FYDPLV-Z
 X-FYDPLVF-Z
 30 X-FYDPLVFP-Z
 X-FYDPLVFPS-Z
 X-FYDPLVFPSD-Z
 X-FYDPLVFPSDE-Z
 X-FYDPLVFPSDEF-Z
 X-FYDPLVFPSDEFD-Z
 X-FYDPLVFPSDEFDA-Z
 35 X-FYDPLVFPSDEFDAS-Z
 X-FYDPLVFPSDEFDASI-Z

X-FYDPLVFPSDEFDASIS-Z
 X-FYDPLVFPSDEFDASISQ-Z
 X-FYDPLVFPSDEFDASISQV-Z
 X-FYDPLVFPSDEFDASISQVN-Z
 X-FYDPLVFPSDEFDASISQVNE-Z
 X-FYDPLVFPSDEFDASISQVNEK-Z
 X-FYDPLVFPSDEFDASISQVNEKI-Z
 5 X-FYDPLVFPSDEFDASISQVNEKIN-Z
 X-FYDPLVFPSDEFDASISQVNEKINQ-Z
 X-FYDPLVFPSDEFDASISQVNEKINQS-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSL-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLA-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLAF-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLAFI-Z
 10 X-FYDPLVFPSDEFDASISQVNEKINQSLAFIR-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRK-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKS-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSD-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDE-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDEL-Z
 X-FYDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z, or

15 X-DELL-Z
 X-SDELL-Z
 X-KSDELL-Z
 X-RKSDELL-Z
 X-IRKSDELL-Z
 X-FIRKSDELL-Z
 X-AFIRKSDELL-Z
 X-LAFIRKSDELL-Z
 X-SLAFIRKSDELL-Z
 X-QSLAFIRKSDELL-Z
 X-NQSLAFIRKSDELL-Z
 X-INQSLAFIRKSDELL-Z
 X-KINQSLAFIRKSDELL-Z
 X-EKINQSLAFIRKSDELL-Z
 X-NEKINQSLAFIRKSDELL-Z
 20 X-VNEKINQSLAFIRKSDELL-Z
 X-QVNEKINQSLAFIRKSDELL-Z
 X-SQVNEKINQSLAFIRKSDELL-Z
 X-ISQVNEKINQSLAFIRKSDELL-Z
 X-SISQVNEKINQSLAFIRKSDELL-Z
 X-ASISQVNEKINQSLAFIRKSDELL-Z
 X-DASISQVNEKINQSLAFIRKSDELL-Z
 25 X-FDASISQVNEKINQSLAFIRKSDELL-Z
 X-EFDASISQVNEKINQSLAFIRKSDELL-Z
 X-DEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-SDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-PSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-FPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-VFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-LVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 30 X-PLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-DPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z

35 X-PLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z
 X-DPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z

X-YDPLVFPSDEFDASISQVNEKINQSLAFIRKSDELL-Z

in which:

amino acid residues are presented by the single-letter code;

5 X comprises an amino group, an acetyl group, a 9-fluoromethyoxyethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

10 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

15 15. A peptide having a formula selected from the group consisting of:

15 X-ITL-Z
X-ITLN-Z
X-ITLNN-Z
X-ITLNNS-Z
X-ITLNNSV-Z
X-ITLNNSVA-Z
20 X-ITLNNSVAL-Z
X-ITLNNSVALD-Z
X-ITLNNSVALDP-Z
X-ITLNNSVALDPI-Z
X-ITLNNSVALDPID-Z
X-ITLNNSVALDPIDI-Z
X-ITLNNSVALDPIDIS-Z
X-ITLNNSVALDPIDISI-Z
25 X-ITLNNSVALDPIDISIE-Z
X-ITLNNSVALDPIDISIEL-Z
X-ITLNNSVALDPIDISIELN-Z
X-ITLNNSVALDPIDISIELNK-Z
X-ITLNNSVALDPIDISIELNKA-Z
X-ITLNNSVALDPIDISIELNKAK-Z
X-ITLNNSVALDPIDISIELNKAKS-Z
30 X-ITLNNSVALDPIDISIELNKAKD-Z
X-ITLNNSVALDPIDISIELNKAKSLE-Z
X-ITLNNSVALDPIDISIELNKAKSLEE-Z
X-ITLNNSVALDPIDISIELNKAKSLEES-Z
X-ITLNNSVALDPIDISIELNKAKSLEESK-Z
X-ITLNNSVALDPIDISIELNKAKSLEESKE-Z
X-ITLNNSVALDPIDISIELNKAKSLEESKEW-Z
35 X-ITLNNSVALDPIDISIELNKAKSLEESKEWI-Z
X-ITLNNSVALDPIDISIELNKAKSLEESKEWIR-Z

X-ITLNNSVALDPIDISIELNKAKSDEESKEWIRR-Z
 X-ITLNNSVALDPIDISIELNKAKSDEESKEWIRRS-Z, or

X-RRS-Z
 X-IRRS-Z
 X-WIRRS-Z
 X-EWIRRS-Z
 X-KEWIRRS-Z
 X-SKEWIRRS-Z
 X-ESKEWIRRS-Z
 X-EESKEWIRRS-Z
 X-LEESKEWIRRS-Z
 X-DLEESKEWIRRS-Z
 X-SDLEESKEWIRRS-Z
 X-KSDLEESKEWIRRS-Z
 X-AKSDLEESKEWIRRS-Z
 X-KAKSDLEESKEWIRRS-Z
 X-NKAKSDLEESKEWIRRS-Z
 X-LNKAKSDEESKEWIRRS-Z
 X-ELNKAKSDEESKEWIRRS-Z
 X-IELNKAKSDEESKEWIRRS-Z
 X-SIELNKAKSDEESKEWIRRS-Z
 X-ISIELNKAKSDEESKEWIRRS-Z
 X-DISIELNKAKSDEESKEWIRRS-Z
 X-IDISIELNKAKSDEESKEWIRRS-Z
 X-PIDISIELNKAKSDEESKEWIRRS-Z
 X-DPIDISIELNKAKSDEESKEWIRRS-Z
 X-LDPIDISIELNKAKSDEESKEWIRRS-Z
 X-ALDPIDISIELNKAKSDEESKEWIRRS-Z
 X-VALDPIDISIELNKAKSDEESKEWIRRS-Z
 X-SVALDPIDISIELNKAKSDEESKEWIRRS-Z
 X-NSVALDPIDISIELNKAKSDEESKEWIRRS-Z
 X-NNSVALDPIDISIELNKAKSDEESKEWIRRS-Z
 X-LNNSVALDPIDISIELNKAKSDEESKEWIRRS-Z
 X-TLNNSVALDPIDISIELNKAKSDEESKEWIRRS-Z

in which:

25 amino acid residues are presented by the single-letter code;

X comprises an amino group, an acetyl group, a 9-fluoromethoxyethyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

30 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

35

16. A peptide having a formula selected from the group consisting of:

X-ALG-Z
 X-ALGV-Z
 X-ALGVA-Z
 X-ALGVAT-Z
 5 X-ALGVATS-Z
 X-ALGVATSA-Z
 X-ALGVATSAQ-Z
 X-ALGVATSAQI-Z
 X-ALGVATSAQIT-Z
 X-ALGVATSAQITA-Z
 X-ALGVATSAQITAA-Z
 10 X-ALGVATSAQITAAV-Z
 X-ALGVATSAQITAAVA-Z
 X-ALGVATSAQITAVAL-Z
 X-ALGVATSAQITAVALV-Z
 X-ALGVATSAQITAVALVE-Z
 X-ALGVATSAQITAVALVEA-Z
 X-ALGVATSAQITAVALVEAK-Z
 X-ALGVATSAQITAVALVEAKQ-Z
 15 X-ALGVATSAQITAVALVEAKQA-Z
 X-ALGVATSAQITAVALVEAKQAR-Z
 X-ALGVATSAQITAVALVEAKQARS-Z
 X-ALGVATSAQITAVALVEAKQARSD-Z
 X-ALGVATSAQITAVALVEAKQARSDI-Z
 X-ALGVATSAQITAVALVEAKQARSDIE-Z
 X-ALGVATSAQITAVALVEAKQARSDIEK-Z
 20 X-ALGVATSAQITAVALVEAKQARSDIEKL-Z
 X-ALGVATSAQITAVALVEAKQARSDIEKLK-Z
 X-ALGVATSAQITAVALVEAKQARSDIEKLKE-Z
 X-ALGVATSAQITAVALVEAKQARSDIEKLKEA-Z
 X-ALGVATSAQITAVALVEAKQARSDIEKLKEAI-Z
 X-ALGVATSAQITAVALVEAKQARSDIEKLKEAIR-Z
 X-ALGVATSAQITAVALVEAKQARSDIEKLKEAIRD-Z, or

 25 X-IRD-Z
 X-AIRD-Z
 X-EAIRD-Z
 X-KEAIRD-Z
 X-LKEAIRD-Z
 X-KLKEAIRD-Z
 X-EKLKEAIRD-Z
 X-IEKLKEAIRD-Z
 X-DIEKLKEAIRD-Z
 30 X-SDIEKLKEAIRD-Z
 X-RSDIEKLKEAIRD-Z
 X-ARSDIEKLKEAIRD-Z
 X-QARSDIEKLKEAIRD-Z
 X-KQARSDIEKLKEAIRD-Z
 X-AKQARSDIEKLKEAIRD-Z
 35 X-EAKQARSDIEKLKEAIRD-Z
 X-VEAKQARSDIEKLKEAIRD-Z

X-LVEAKQARS DIEKLKEAIRD-Z
X-ALVEAKQARS DIEKLKEAIRD-Z
X-VALVEAKQARS DIEKLKEAIRD-Z
X-AVALVEAKQARS DIEKLKEAIRD-Z
X-AAVALVEAKQARS DIEKLKEAIRD-Z
X-TAAVALVEAKQARS DIEKLKEAIRD-Z
X-ITAAVALVEAKQARS DIEKLKEAIRD-Z
5 X-QITAVALVEAKQARS DIEKLKEAIRD-Z
X-AQITAVALVEAKQARS DIEKLKEAIRD-Z
X-SAQITAVALVEAKQARS DIEKLKEAIRD-Z
X-TSAQITAVALVEAKQARS DIEKLKEAIRD-Z
X-ATSAQITAVALVEAKQARS DIEKLKEAIRD-Z
X-VATSAQITAVALVEAKQARS DIEKLKEAIRD-Z
10 X-GVATSAQITAVALVEAKQARS DIEKLKEAIRD-Z
X-LGVATSAQITAVALVEAKQARS DIEKLKEAIRD-Z

10 in which:

amino acid residues are presented by the single-letter code;

15 X comprises an amino group, an acetyl group, a 9-fluoromethyoxy-methyl-carbonyl group, a hydrophobic group, or a macromolecule carrier group;

20 Z comprises a carboxyl group, an amido group, a hydrophobic group, or a macromolecular carrier group.

17. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein X is a hydrophobic group.

25 18. The peptide of Claim 17 wherein the hydrophobic group X is carbobenzoyl, dansyl, or t-butyloxycarbonyl.

30 19. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein Z is a hydrophobic group.

20. The peptide of Claim 19 wherein the hydrophobic group Z is t-butyloxycarbonyl.

35

21. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein X is a macromolecular carrier group.

22. The peptide of Claim 21 wherein the macromolecular carrier group is a lipid-fatty acid 5 conjugate, a polyethylene glycol, or a carbohydrate moiety.

23. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein Z is a macromolecular carrier group. 10

24. The peptide of Claim 23 wherein the macromolecular carrier group Z is a lipid-fatty acid conjugate, a polyethylene glycol, or a carbohydrate moiety. 15

25. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein at least one bond linking adjacent amino acid residues is a non-peptide bond.

20 26. The peptide of Claim 25 wherein the non-peptide bond is an inino, ester, hydrazine, semicarbazide, or azo bond.

25 27. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein at least one amino acid residue is in a D-isomer configuration.

30 28. The peptide of Claim 11, 12, 13, 14, 15 or 16 further comprising at least one amino acid insertion.

35 29. The peptide of Claim 11, 12, 13, 14, 15 or 16 wherein the amino acid insertion is between 1 and 15 amino acid residues.

30. The peptide of Claim 11, 12, 13, 14, 15 or 16 having at least one less amino acid residue, wherein the amino acid residue(s) represents an amino acid deletion, and wherein the peptide comprises at least three amino acid residues.

5

31. The peptide of Claim 11, 12, 13, 14, 15 or 16 further comprising at least one amino acid substitution wherein a first amino acid residue is substituted for a second, different amino acid residue.

10

32. The peptide of Claim 31 wherein the amino acid substitution is a conserved substitution.

15

33. The peptide of Claim 31 wherein the amino acid substitution is a non-conserved substitution.

20

34. A method for the inhibition of transmission of an enveloped virus to a cell, comprising contacting the cell with an effective concentration of the peptide of Claim 1 for an effective period of time so that no infection of the cell by the virus occurs.

25

35. A method for neutralizing an enveloped virus in a host, comprising administering to the host an effective concentration of the peptide of Claim 1 so that the host raises an immune response sufficient to neutralize the virus, and viral infection of uninfected cells in the host is inhibited.

30

35

36. A method for neutralizing an enveloped virus in a host, comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 1 so that viral infection of uninfected cells in the host is inhibited.

37. A method for the detection of an enveloped virus comprising:

5 contacting a viral isolate with an effective concentration of the peptide of Claim 1 for an effective amount of time so that viral infectivity is inhibited; and

assaying the viral isolate for viral enzyme activity.

10 38. A method for the inhibition of transmission of an HIV retrovirus to a cell, comprising contacting the cell with an effective concentration of the peptide of Claim 11 or 12 for an effective period of time so that no infection of the cell by the retrovirus occurs.

15

20 39. A method for neutralizing an HIV retrovirus in a host, comprising administering to the host an effective concentration of the peptide of Claim 11 or 12 so that the host raises an immune response sufficient to neutralize the HIV retrovirus, and HIV infection of uninfected cells in the host is inhibited.

25 40. A method for neutralizing an HIV retrovirus in a host, comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 11 or 12 so that HIV infection of uninfected cells in the host is inhibited.

30

41. A method for the detection of HIV, comprising:

35 contacting a viral isolate with an effective concentration of the peptide of Claim 11 or 12 for an effective amount of time so that HIV viral infectivity is inhibited; and

assaying the viral isolate for retroviral enzyme activity.

42. A method for the inhibition of transmission of a respiratory syncytial virus to a cell, comprising
5 contacting the cell with an effective concentration of the peptide of Claim 13 or 14 for an effective period of time so that no infection of the cell by the virus occurs.

10 43. A method for neutralizing a respiratory syncytial virus in a host, comprising administering to the host an effective concentration of the peptide of Claim 13 or 14 so that the host raises an immune response sufficient to neutralize the virus, and
15 respiratory syncytial virus infection of uninfected cells in the host is inhibited.

20 44. A method for neutralizing a respiratory syncytial virus in a host comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 13 or 14 so that respiratory syncytial virus infection of uninfected cells in the host is inhibited.

25 45. A method for the detection of respiratory syncytial virus comprising:
contacting a viral isolate with an effective concentration of the peptide of Claim 13 or 14 for an effective amount of time so that respiratory syncytial
30 viral infectivity is inhibited; and
assaying the viral isolate for respiratory syncytial virus enzyme activity.

35 46. A method for the inhibition of transmission of a parainfluenza virus to a cell comprising,

contacting the cell with an effective concentration of the peptide of Claim 15 or 16 for an effective period of time so that no infection of the cell by the virus occurs.

5 47. A method for neutralizing a parainfluenza virus in a host, comprising administering to the host an effective concentration of the peptide of Claim 15 or 16 so that the host raises an immune response sufficient to neutralize the virus, and parainfluenza 10 infection of uninfected cells in the host is inhibited.

15 48. A method for neutralizing a parainfluenza virus in a host comprising administering to the host an effective concentration of an antibody raised against the peptide of Claim 15 or 16 so that parainfluenza infection of uninfected cells in the host is inhibited.

20 49. A method for the detection of parainfluenza virus comprising:

 contacting a viral isolate with an effective concentration of the peptide of Claim 15 or 16 for an effective amount of time so that parainfluenza viral 25 infectivity is inhibited; and

 assaying the viral isolate for parainfluenza virus enzyme activity.

30

35

HIV1LAI (DP-178; SEQ ID:1)	YTSLIHSLIEESQNQQEKNEQELLELDKWA SLWNMF
HIV1SF2 (DP-185; SEQ ID:3)	YTNTIYNLLEESQNQQEKNEQELLELDKWA SLWNMF
HIV1RF (SEQ ID:4)	YT CI IYNLLEESQNQQEKNEQELLELDKWA NLWNMF
HIV1MN (SEQ ID:5)	YTSLIYSLEKSQTQQEKNEQELLELDKWA SLWNMF
HIV2R0D (SEQ ID:6)	LEANISKSLEQAQIQQEKNM YELQ KLNSWDIFGNMF
HIV2NIHZ (SEQ ID:7)	LEANISQSLEQAQIQQEKNM YELQ KLNSWDVF TNWL
DP180 (SEQ ID:2)	SSESFTLLEQ WNN KLQLAEQ W LEQ Q INEKHYLEDIS
DP118 (SEQ ID:10)	QQLLDVVKRQQEMRLRTW W TKNLQARVTAIEKYLLKDQ
DP125 (SEQ ID:8)	CGGNM W LLRAIEAQ Q HLQLQTW W IKQLQARILAVERYLKDQ
DP116 (SEQ ID:9)	LQARILAVERYLKDQ QQ

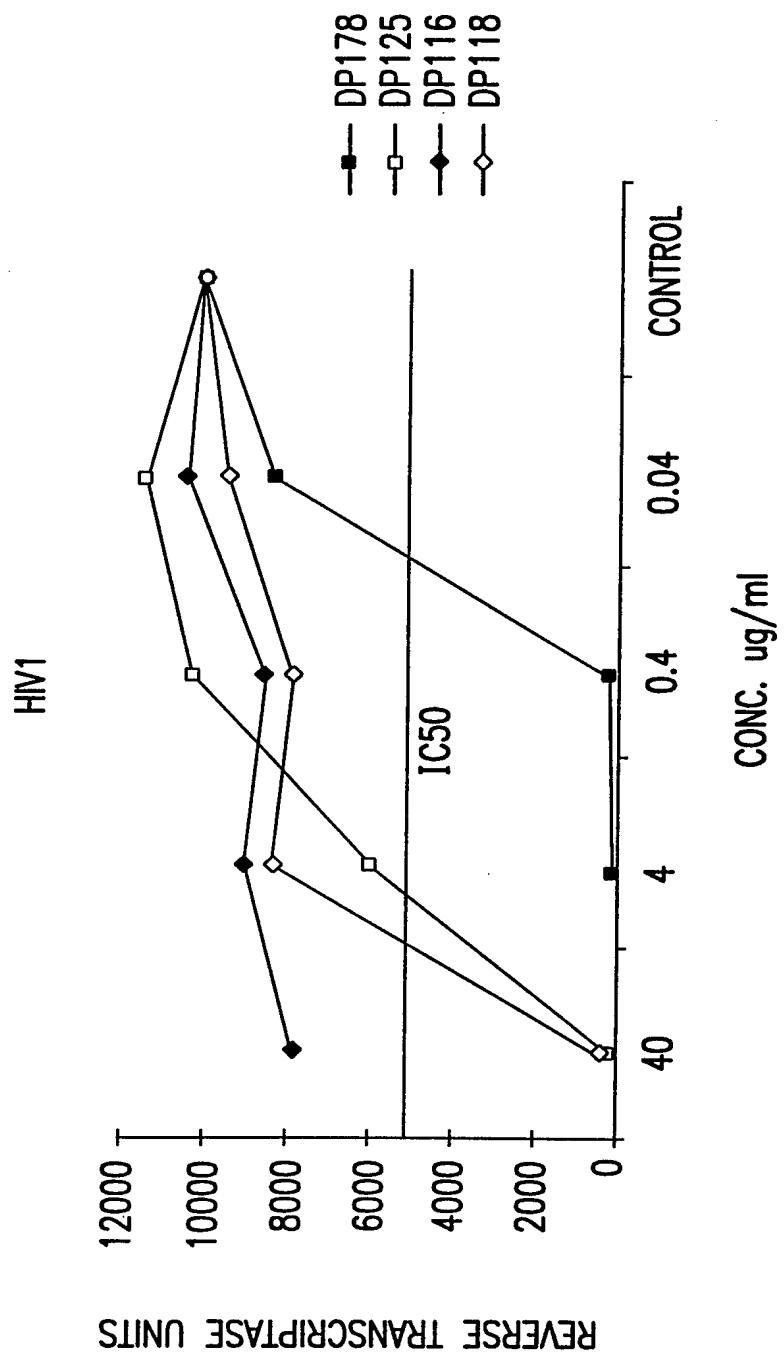
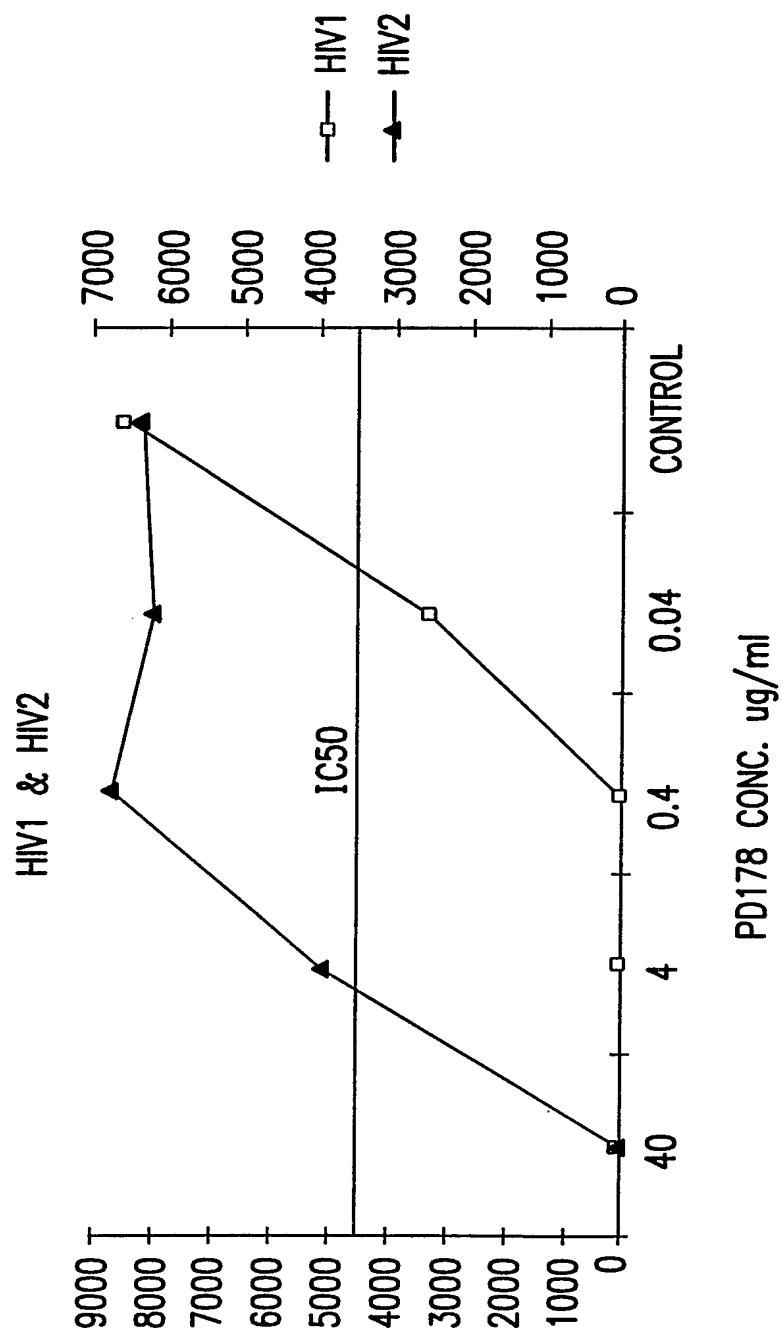


FIG. 2



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FIG. 3

Number of Syncytia/well: concentration in $\mu\text{g}/\text{ml}$ (micrograms/ml)									
DP178	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control
<i>Syncytia</i>									
HIV1LAI	0	0	0	0	0	0	0	0	67
HIV1MN	0	0	0	0	0	ND	ND	ND	34
HIV1RF	0	0	0	0	0	ND	ND	ND	65
HIV1SF2	0	0	0	0	0	ND	ND	ND	58
DP125	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control
<i>Syncytia</i>									
HIV1LAI	0	0	54	69	80	75	79	82	67
HIV1MN	0	0	30	36	ND	ND	ND	ND	34
HIV1RF	0	0	67	63	ND	ND	ND	ND	65
HIV1SF2	0	0	9	66	ND	ND	ND	ND	58
DP116	10	5	1	0.2	0.1	0.05	0.025	0.0125	Control
<i>Syncytia</i>									
HIV1LAI	75	ND	ND	ND	ND	ND	ND	ND	67
HIV1MN	35	ND	ND	ND	ND	ND	ND	ND	34
HIV1RF	81	ND	ND	ND	ND	ND	ND	ND	65
HIV1SF2	81	ND	ND	ND	ND	ND	ND	ND	58

FIG.4A

DP180	40	20	10	5	2.5	1.25	0.625	0.3125	Control
<i>Syncytia</i>									
HIV1LAI	50	>45	>45	>45	>45	>45	>45	>45	58
<i>Syncytia</i>									
DP185	40	20	10	5	2.5	1.25	0.625	0.3125	Control
HIV1LAT	0	0	0	0	0	0	0	ND	60

FIG.4B
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HIV1Number of Syncytia/well: concentration in ng/ml (nanograms/ml)

DP178	20	10	5	2.5	1.25	0.625	0.3125	Control
<i>Syncytia</i>								
HIV1	0	0	0	0	0	14	20	48
<u>DP116</u>								
<i>Syncytia</i>	20	10	5	2.5	1.25	0.625	0.3125	Control
HIV1	ND	48	ND	ND	ND	ND	ND	ND

HIV2Number of Syncytia/well: concentration in μ g/ml (micrograms/ml)

DP178	20	10	5	2.5	1.25	0.625	0.3125	Control
<i>Syncytia</i>								
HIV2	50	54	55	57	63	77	78	76
<u>DP116</u>								
<i>Syncytia</i>	20	10	5	2.5	1.25	0.625	0.3125	Control
HIV2	ND	58	ND	ND	ND	ND	ND	ND

FIG.5

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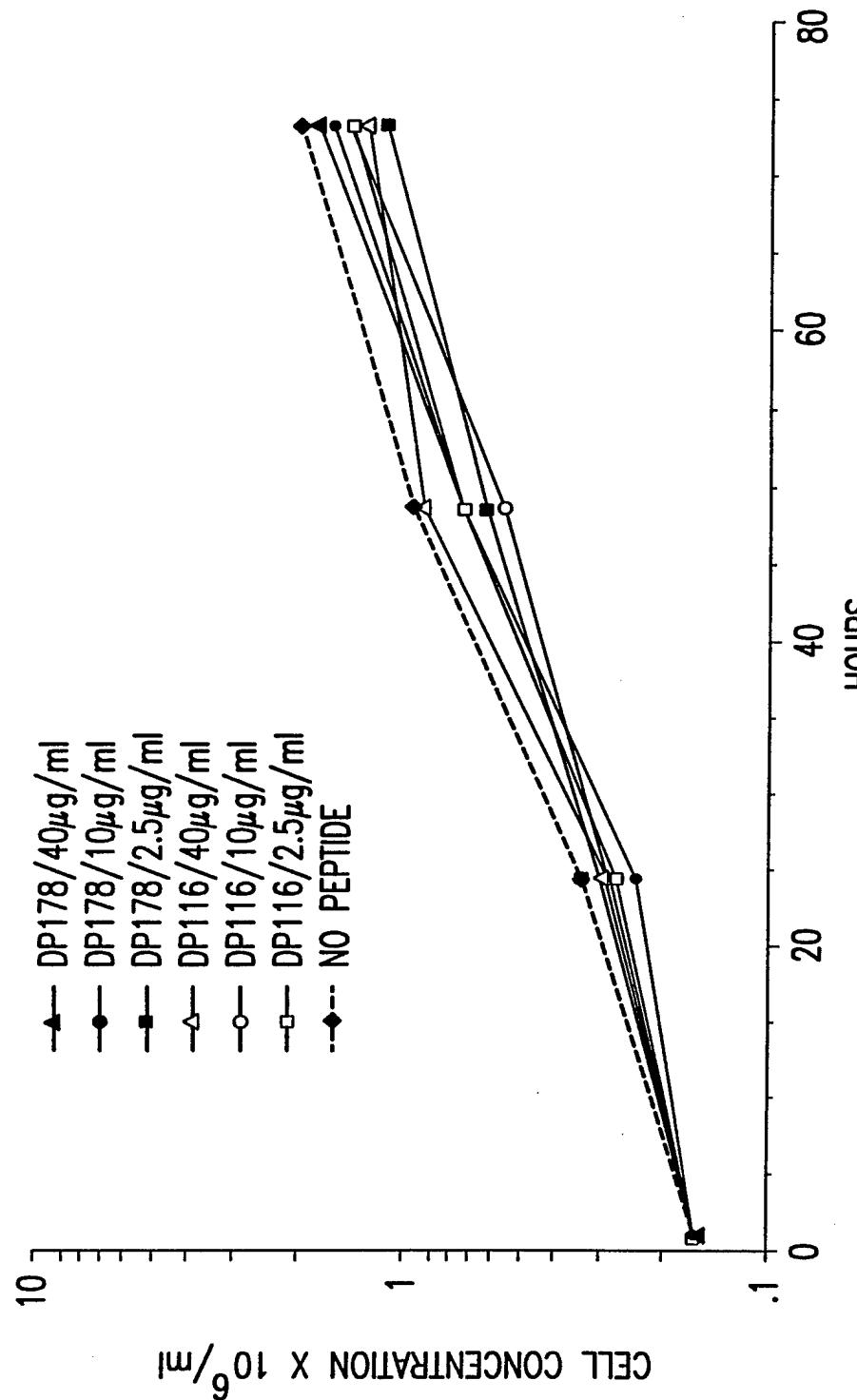
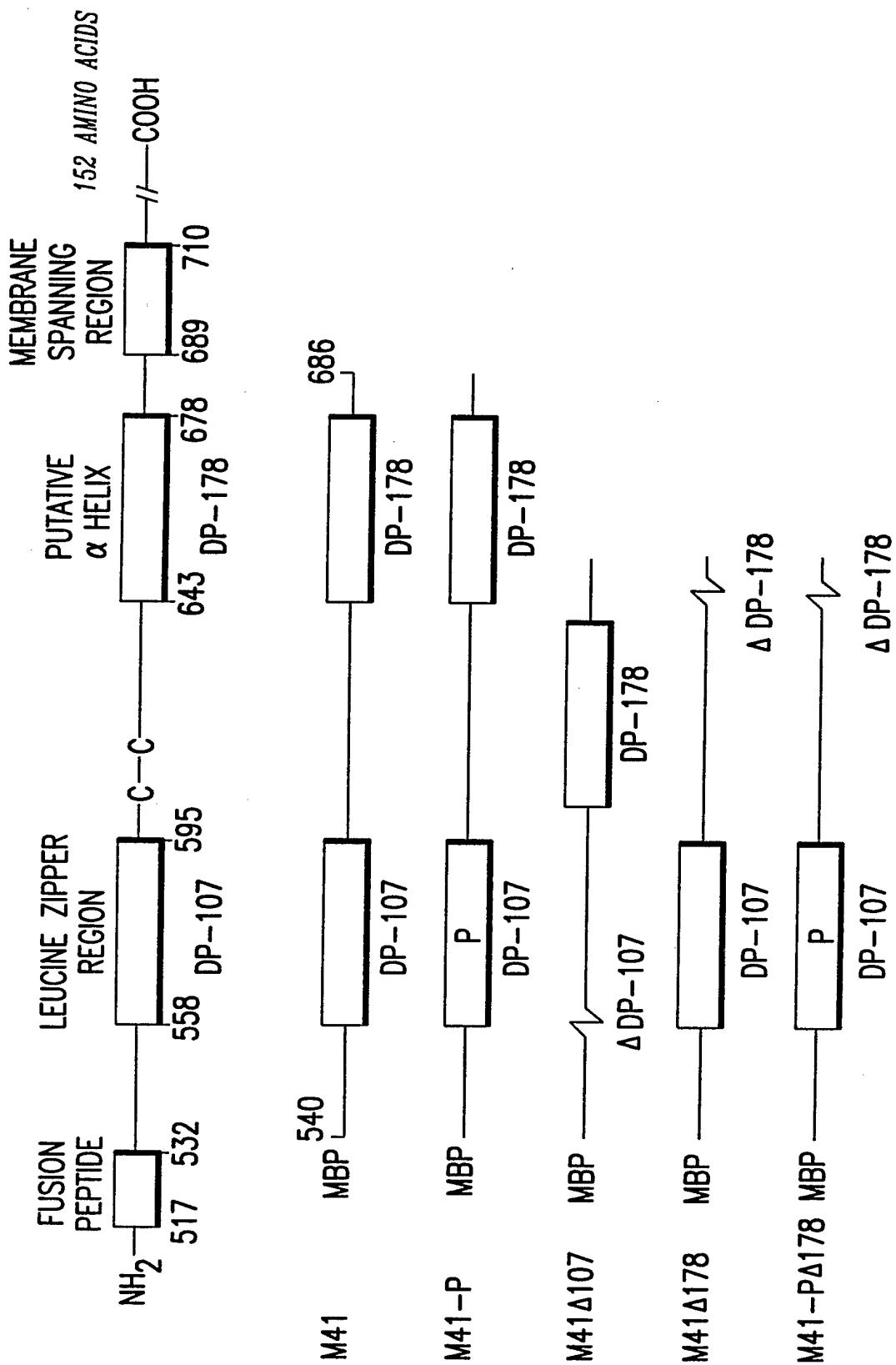


FIG. 6



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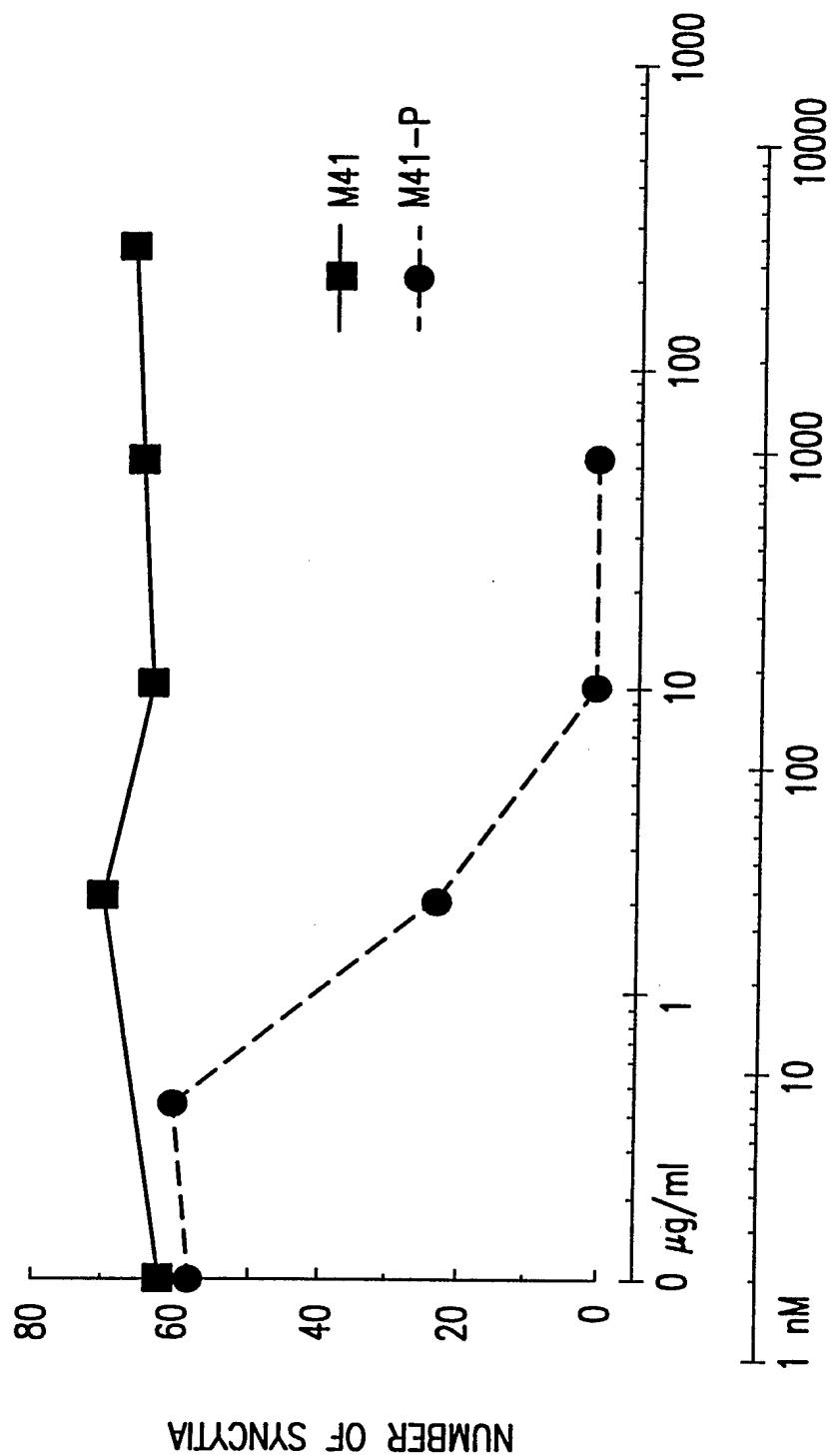


FIG. 8

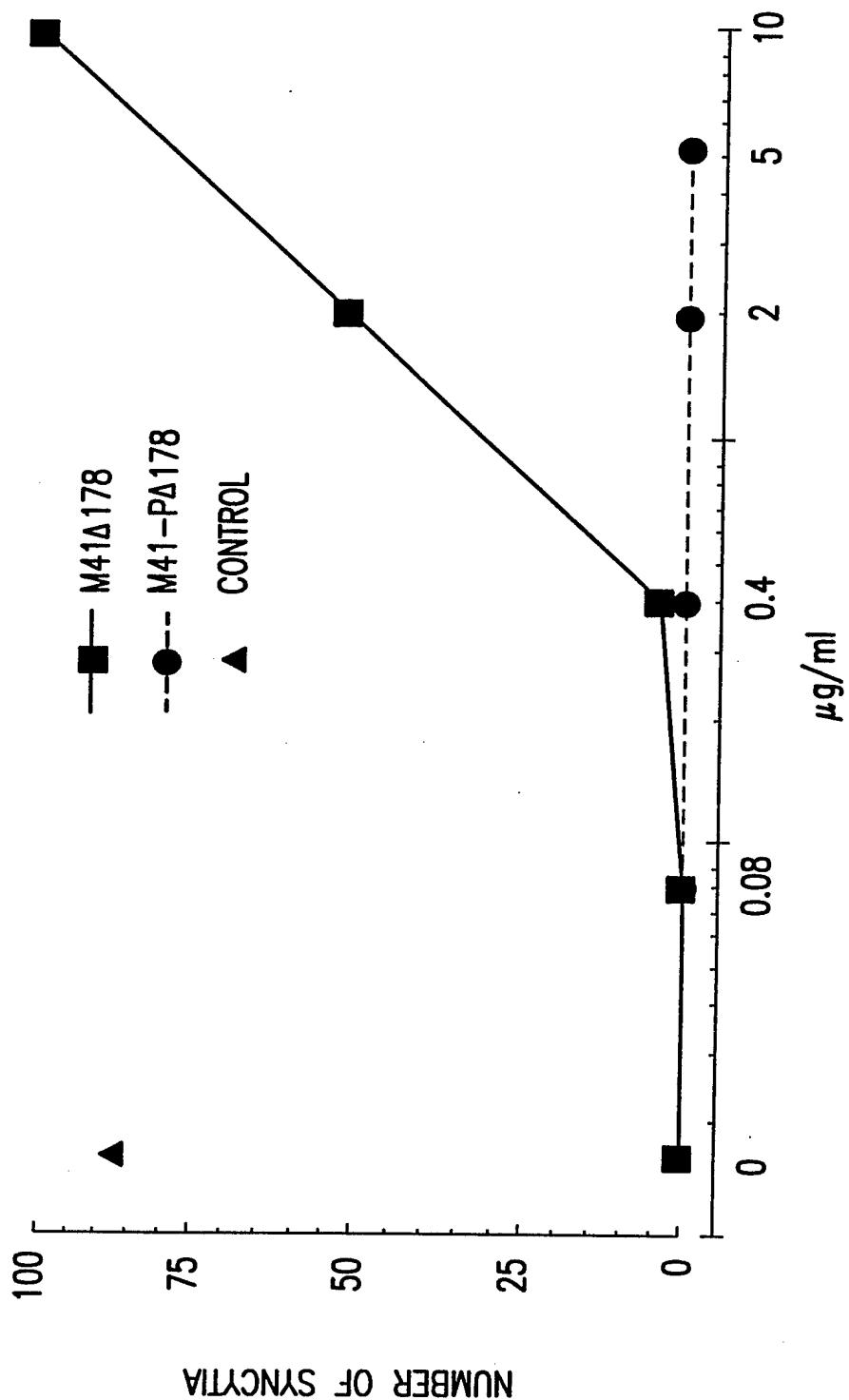


FIG. 9

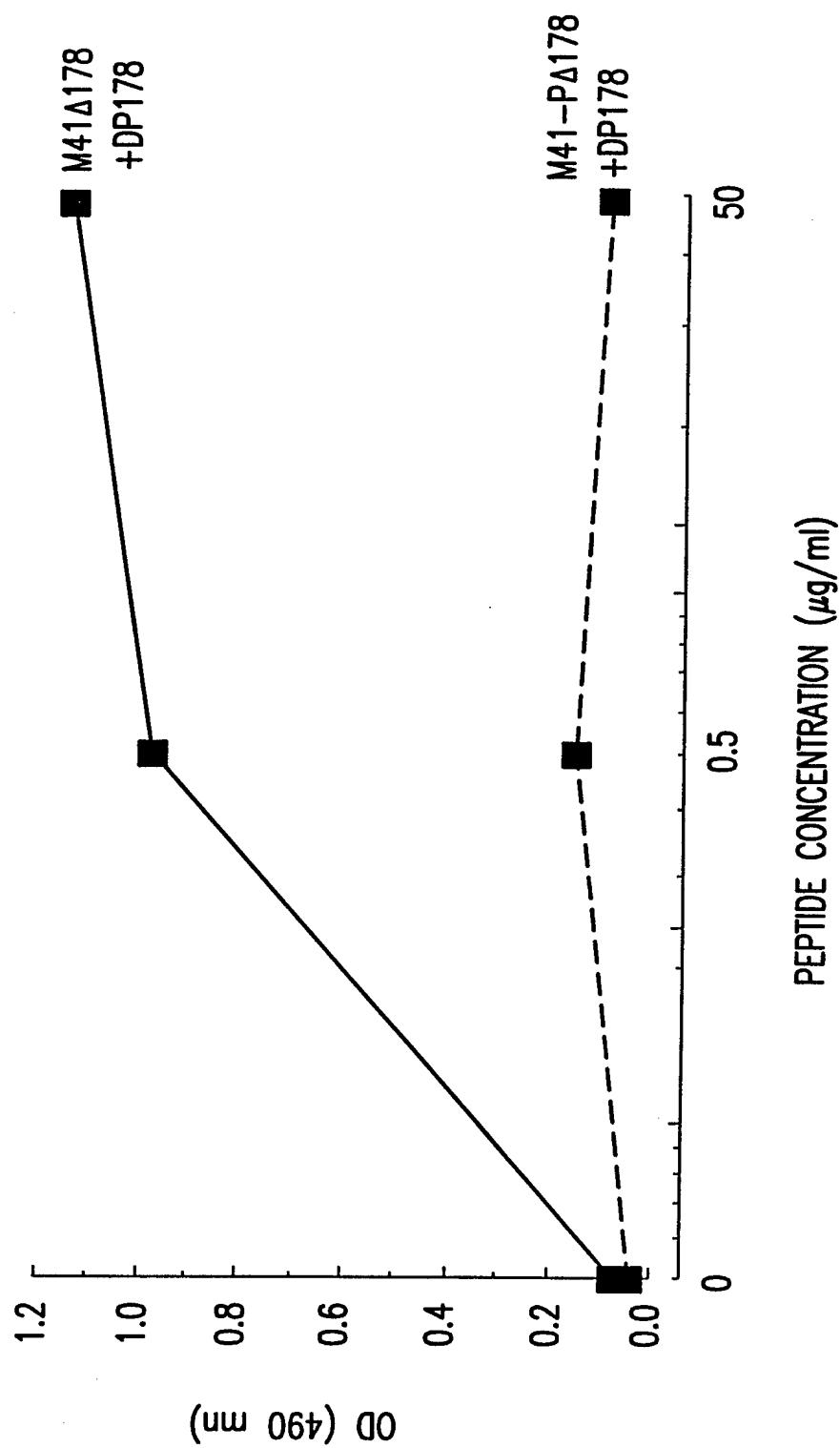


FIG.10

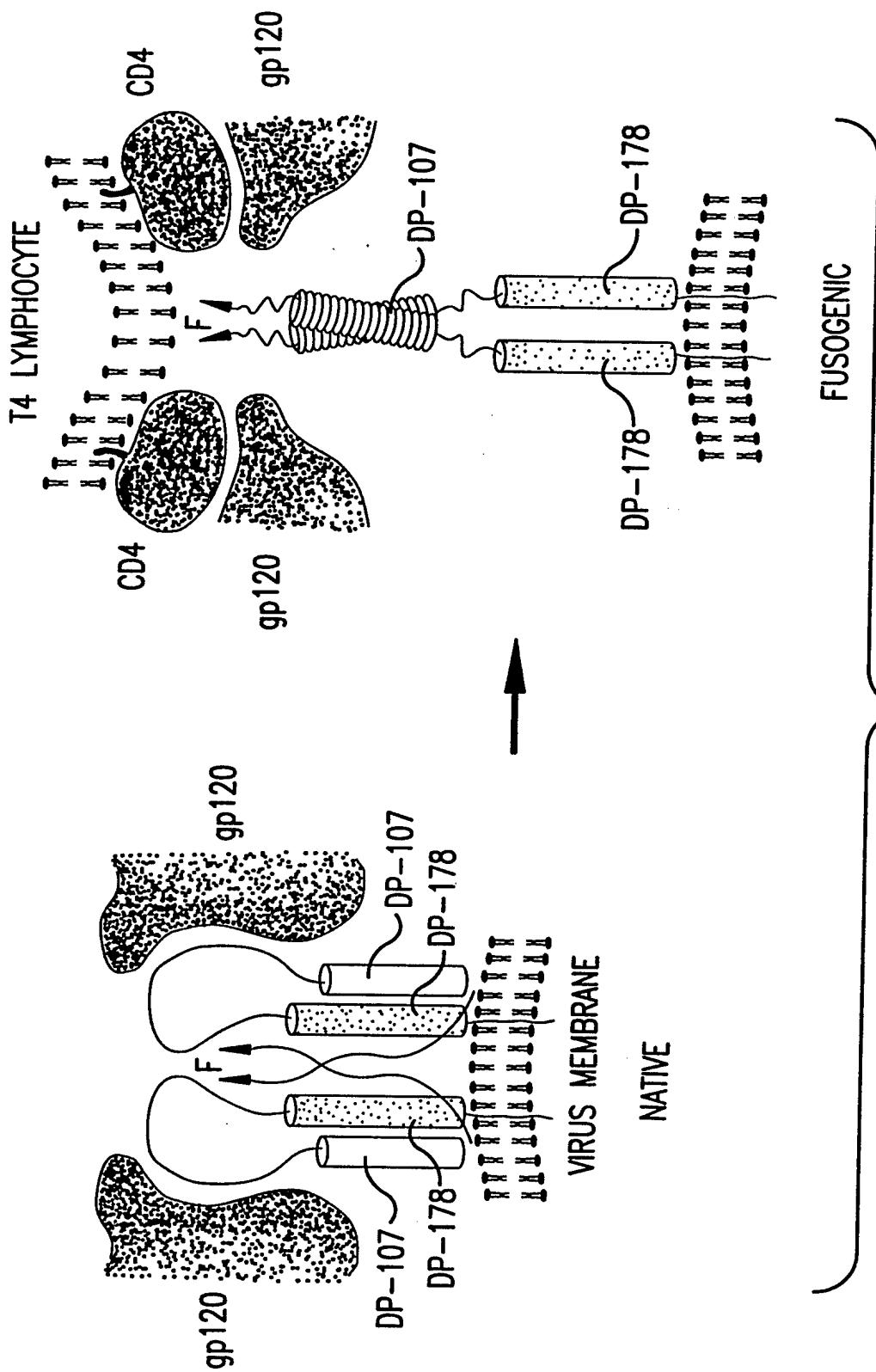


FIG. 11A

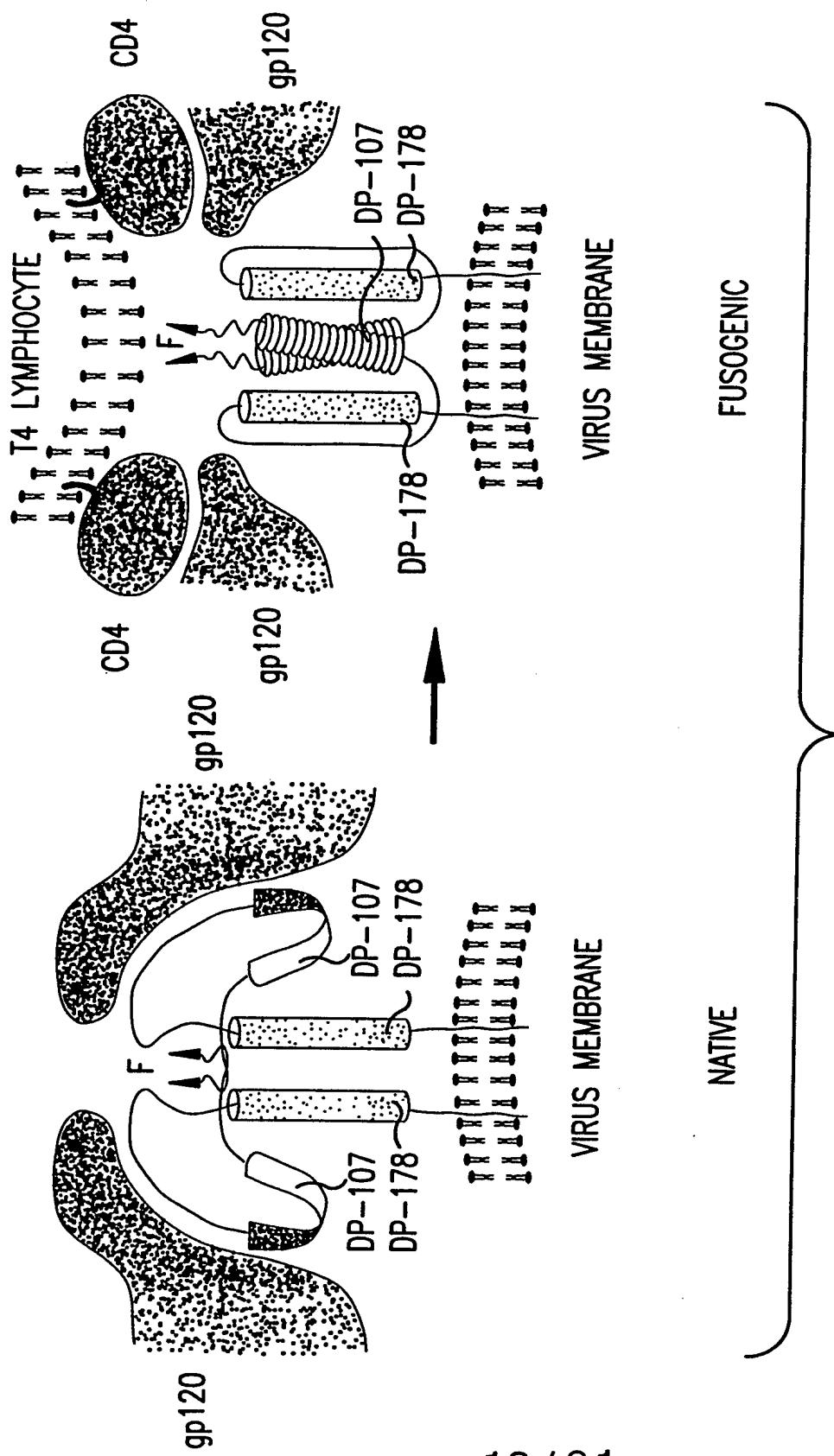


FIG. 11B

Sequence	Positions								Motifs
	A	D	A	D	A	D	A	D	
GCN4 (gcn4 yeast)	M	K	Q	L	E	D	K	V	[LMNV] {CFGIMPWTW}
C-FOS (fos_human)	T	D	T	L	Q	A	E	T	[IKL] {CFGHIMP RWY}
C-JUN (top1_human)	I	A	R	L	E	E	K	V	[AILNV] {CDFGHILPVWY}
C-MYC (myo_human)	E	Q	K	L	I	S	E	D	[ELR] {ACFGMPWY}
FLU LOOP 36	I	E	K	T	N	E	K	F	[FILT] {ACFLMPTW}

FIG. 12

Sequence	Positions												Motifs	
	D	A	D	A	D	A	D	A	D	A	D	A		
DP-107 (env_hv1bru)Y1=D	N	N	L	R	A	I	E	A	Q	H	L	Q	L	[ILQT] {CFIMPSTY}
DP-107 (env_hv1bru)Y1=D	N	N	L	R	A	I	E	A	Q	H	L	Q	L	[ILQT] {CDFIMPST}
DP-107 (env_hv1bru)Y1=D	N	N	L	R	A	I	E	A	Q	H	L	Q	L	[ILQT] {CDFIMPST}
DP-107 (env_hv1bru)Y1=D	N	N	L	R	A	I	E	A	Q	H	L	Q	L	[ILQT] {CDFIMPSTY}
DP-107 (env_hv1bru)Y2=D	N	N	L	R	A	I	E	A	Q	H	L	Q	L	[EKLNQV] {CDFKMPSVY}
DP-107 (env_hv1bru)Y2=D	N	N	L	R	A	I	E	A	Q	H	L	Q	L	[EKLNQV] {CDFKMPSY}
DP-107 (env_hv1bru)Y2=D	N	N	L	R	A	I	E	A	Q	H	L	Q	L	[EKLNQV] {CFKMPY}
DP-107 (env_hv1bru)Y2=D	N	N	L	R	A	I	E	A	Q	H	L	Q	L	[EKLNQV] {CFKMPSY}
DP-178 (env_hv1bru)Y1=A	Y	I	S	L	I	E	S	Q	N	Q	E	K	N	[EKLQY] {ACFGMPRWWY}
DP-178 (env_hv1bru)Y1=A	Y	I	S	L	I	E	S	Q	N	Q	E	K	N	[EKLQWY] {ACFGMPRVY}
DP-178 (env_hv1bru)Y1=A	Y	I	S	L	I	E	S	Q	N	Q	E	K	N	[EKLQWY] {ACFGMPRYY}
DP-178 (env_hv1bru)Y1=D	Y	T	S	L	I	H	S	L	I	E	S	Q	N	[EILNQSY] {ACFGMPRWWY}
DP-178 (env_hv1bru)Y1=D	Y	T	S	L	I	H	S	L	I	E	S	Q	N	[EILNQSY] {ACFGMPRVY}
DP-178 (env_hv1bru)Y1=D	Y	T	S	L	I	H	S	L	I	E	S	Q	N	[EILNQSY] {ACFGMPRYY}

FIG. 13

FIG. 14

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SUBSTITUTE SHEET (RULE 26)

FIG. 15

Sequence	Positions										Parent Motif	Hybrid Motif	
	A	D	A	D	A	D	A	D	A	D			
DP-107 (env_hv1bru)1=D	N	N	R	A	A	Q	H	L	Q	T	W	G	[LQLQV] {CDF IMPST}
DP-107 (env_hv1bru)2=D	N	N	R	A	I	E	A	Q	H	L	Q	I	[EKLNQV] {CFKNPQS}
DP-178 (env_hv1bru)Y1=A	Y	T	S	L	I	H	S	L	I	E	S	Q	[EFKLQWY] {FCFGMPRVY}
DP-178 (env_hv1bru)Y1=D	Y	T	S	L	I	H	S	L	I	E	S	Q	[EFILNQSY] {FCGMPRVY}
FLU LOOP 36	I	E	K	T	N	E	K	F	H	Q	I	E	[EFILNQSTWVY] {FCGMP}
													[FLTV] {ACFLMPPTWV}

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SUBSTITUTE SHEET (RULE 26)

FIG. 16

Sequence	Positions						Parent Motif	Hybrid Motif
	A	D	A	D	A	D		
GCN4 (gcn4 yeast) DP-107 (env_hv1brv) L1=D DP-178 (env_hv1brv) Y1=A	M K Q L E D K V E E L L S K N Y H L E N E V A R I L K K L						[LMNV] {CFGIMPW} [ILQTV] {CDFIMPST} [EFKLQWY] {CFGMPRVY}	[EFIKLMNQTVWY] {CFMP}
GCN4 (gcn4 yeast) DP-107 (env_hv1brv) L1=D DP-178 (env_hv1brv) Y1=D	M K Q L E D K V E E L L S K N Y H L E N E V A R I L K K L						[LMNV] {CFGIMPW} [ILQTV] {CDFIMPST} [EFILNQSYW] {CFGMPRVY}	[EFIKLMNQRTSYWY] {CFMP}
GCN4 (gcn4 yeast) DP-107 (env_hv1brv) L2=D DP-178 (env_hv1brv) Y1=A	M K Q L E D K V E E L L S K N Y H L E N E V A R I L K K L						[LMNV] {CFGIMPW} [EKLNQV] {CFKMPS} [EFKLQWY] {CFGMPRVY}	[EFIKLMNQWY] {CFMP}
GCN4 (gcn4 yeast) DP-107 (env_hv1brv) L2=D DP-178 (env_hv1brv) Y1=D	M K Q L E D K V E E L L S K N Y H L E N E V A R I L K K L						[LMNV] {CFGIMPW} [EKLNQV] {CFKMPS} [EFILNQSYW] {CFGMPRVY}	[EFIKLMNQSYWY] {CFMP}

FIG. 17

FIG. 18

P-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]
P-{P}(1)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(2)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(3)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(4)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(5)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(6)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(7)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(8)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(9)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-{P}(10)-[LIV]-P(6)-[LIV]-P(6)-[LIV]
P-X(1,12)-[LIV]-{P}(6)-[LIV]-P(6)-[LIV]
P-X(13,23)-[LIV]-{P}(6)-[LIV]-{P}(6)-[LIV]

FIG. 19

Fusion Peptide: **♥.....ELGFLG.....♥ ALLMOTIS A AGSTMGARSM TLTQVQARQ** **▲107x178x4▲**
♥.....ELGFLG.....♥ ALLMOTIS A AGSTMGARSM TLTQVQARQ **▲LL SGIVQQQ DP107-NNL**

LRAIEAOQHL LOLTVWGIKO LOARILAYER YLKDO-DP107 OLLG▲▼ I WGC

♦107x178x4♦
LVS Coiled-Coil
SGKLI CT TAVP ♦WNASWS NKSLEQIWNN MTWM *E ♦WDREI NN DP178-

YTSLIHSL IEESONOQEK NEOELLELDK* WASLWNWF-DP178 NI

◆ Transmembrane Region ◆
TNWLWYIK◆ **IF IMIVGGLVGL RIVFAVLSIV** NRVROGYS◆ PL

♦P23LZIPC♦ SFQTHLPTPR GDPR ♦PEGIEE EGGERDRDRS IRLVNGSLAL IWDDLRSL♦ CL.

ALLMOT15 ♠ 107x178x4 ♠
F SYHRLRDLL LIVTRIVELL GRRGW ♠ EALKY WWNLLOYWSO

ELKNSAVSLL NAT ♣ AIAVAEG TDRVIEVVQG A♥ CRAIRHPR

RIRQGLERIL L

FIG. 20

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Fusion **♥ALLMOTI5♥**
 Peptide **♦107x178x4♦**
 ♥.....FLGEL LGVGSAIAS GVA **♦VSKVLHL EGEVNKIKSA**

P1&12LZIPC
LLSTNKAVVS LSNGVSVLTS KVLDLKNYID KQ♦♥ LL ***PIVNKQ**

♦107x178x4♦
 SC **♦SISNIETV I♦ EFOOKNNRLLEITREFSVNAG♦** VTTPVSTMLTNSELLSL

P1&12LZIPC
♥ALLMOTI5♥
 INDM ***PI** **♥TNDQ KKLMSNNVQI V**♦ **RQQSYSI**♦ MS IIKEEVLAYV

 VQ♥ LPLYGVID TPCWKLHTSP LCTTNTKEGS NICLRTDRG WYCDNAGSVS

 FFPQAETCKV QSNRVFCDTM NSLTPSEIN LCNVDIFNPK

 YDCKIMTSKT DVSSSVITSL GAIVSCYGKT KCTASNKNRG

 IIKTFNSNGCDYVSNKGMDTV SVGNTLYYVN KQEGKSLYVK G

P7, 12, & 23LZIPC
♦107x178x4♦ **♥ALLMOTI5♥**
 EPIINFYDPLVF ***PSDE** **♦FDASISQVNEKINQSLAF** **♦I♦ RKSDELL♦**

♦Transmembrane Region♦
HNVNA♦ GK STTN **♦IMITI IIVIVILLS LIAVGLLLY**♦ C♦

 KARSTPVTLS KDQLSGINNI AFSN

FIG. 21

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Fusion
 Peptide **▼ALLMOT15▼ ^{▲107x178x4▲}**
**FLGFLG** **▼AAGTA MGAAA ^{▲TALTVOQSQHLLAGILOQQQKNLLAAV}**

EAQ▲ QQM ^{▲107x178x4▲} LKLTIWGVKNLNARVTALEKYLEDQARLN▲ AWG▼ CA

LVS Coiled-Coil
▼ALLMOT15▼ ^{▲107x178x4▲}
WKQVCHTTVP WQWNNRTPDW ▼NNMT *WLE ^{▲WERQISYLEGNIT}

**^{▲107x178x4▲}
TQLEEARAQEEKNLD▲ AYQKLSS* WSDFWSW▼ FDF ^{▲SKWLN} ^{♦ILK}
 ♦Transmembrane Region♦
IGFLDVVLGIGLRLLYTV♦ YS▲ CIARVRQGYS PLSPQIHIHP WKGQPDNAEG**

PGEGGDKRKN SSEPWQKESG TAEWKSNWCK RLTNWCSISS IWLYNS

**▼ALLMOT15▼
 ▼CLTL LVHLRSAFQY IQYGLGELKA AAQEAVVVALA RLAQNAGYQIWL▼**

ACRSAYRA IINSPRRVRQ GLEGILN

FIG. 22

Fusion ▲107x178x4▲
 Peptide *LVS Coiled-Coil*
FAG *SNLNAQAIQ
VVL AGVALGVATA AQITAGIALHQ *SNLNAQAIQ

SLRTSLEQSNKAIEEIREATQETVIA* VQGVQDY▲ VNNEL VP

ALLMOT15
▲107x178x4▲
P6 & 12LZIPC
AMQHMSCELVGQRLGLRLRYYTELLSIFGPSLRD *PISA *EISIQALIYAL

GGEIHKILEKLGYSGSD▲ MIAILESRGIKTKII THVDLPGKFIILSISY

P1 & 12LZIPC
PTLSEVKGVIVHRLEAV SYNIGSQEWYTTVPRYIATNGYLISNFDESSCVFVS

ESAICSQNSL YPMSPLLQQC IRGDTSSCAR TLVSGTMGNK FILSKGNIVA

NCASILCKCY STSTIINQSP DKLLTFIASD TCPLVEIDGA TIQVGGRQYP

LVS Coiled-Coil
ALLMOT15
P12 & 23LZIPC
DMVYEGKVAL G *PAISLD *RL*DVGTNLGNALKLDDAKVLI*

♦Transmembrane Region♦
DSS♦ NQILETVR RS♦* SFN ♦FGSLL ♦SVPILSCTALALLLIYCC♦
 K RRYQQTLKQH TKVDPAFKPD LTGTSKSYVR SL

FIG. 23

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Fusion ♥ALLMOTI5♥
 Peptide
 ♥.....FIGAI IGSVALGVA TAAQITAASA LIQANQNAAN ♣107x178x4♣
ILRLKESITA

TIEAVHEVTDGLSQLAVA♣ VG KM♥ QQFVNDQFNNTAQELDCIKITQQV

 ♥ALLMOTI5♥
 GVELNLYLTELTTV FGPQITSPAL ♥TQLTIQALYNAGGNMDYLLTKLGVG

 ♦P1 & 12LZIPC♦
 NNQLSSLIGSGLIT GN♥ ♦PILYDSQT QLLGIQVTLV SVGNLNNMRATYLET

 LSVST TKGFASALVP KVVTQVGSVI EELDTSYCIE TDLDLYCTRI VTFPMSPGIY

 SCLNGNTSAC MYSKTEGALT TPYMTLKGSV LANCKMTTCR CADPPGIISQ

 ♥ALLMOTI5♥
 ♣107x178x4♣
 NYGEAVSLID RHSCN ♣♥VSLD GITLRLSGEF DATYQKNISI LDSQVIVTG

 LVS Coiled-Coil
 *NLDISTELGNV NNSISNALDK LEESNSKLDK VNVKLTSTSA ♦Trans-
 ♦LIT* YIA

 membrane Region♦
LTAISLVCGILSLV♥♣ LACYLMLY♦ KQKAQQKTLLWLGNNTLGQMRATTKM

FIG. 24

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Fusion ♥ALLMOTIS♥
Peptide ▲107x178x4▲ *LVS Coiled-Coil*
.....FFGGV ▲IG ♥TIALG *VATSAQITAAVALVEAKOARS DIEKLKE

AIRDTNKAQOSVQSSIGNLIVAIKSVQ* **DYVNKE** ♥ ♣ IVPSIARLGCEAAG

♥ ALLMOTIS ♥
▲ 107x178x4 ▲
LQLGIALTQH ▲ ♥ YSELTNIFGDNIGSLOEKGIKLOGIASLYRTNITE ♥ ▲

IFTTSTVDKYDIYDLLFTESIKVRVIDVDLNDYSITLQVRL **•P5 & 12LZIPC•**
PLLTRLLNTQIYR

VDSISYNI♦ QNREWYI♦ PLPSHIMTKGAFLGGADVKECIEAFSSYIC

PSDPGFVLNHEMESCLSGNISQCPRTVVKSDIVPRYAFVNGGVVANCITT

TCTCNGIGNRINQPPDQGVKIITHKECNTIGINGMLFNTNKEGTLAFYTP

♥ ALLMOT15 ♥
↑107x178x4↑
⊕P6 & 23LZIPC⊕
NDITLNNSVALD ⊕PIDI ↑SIELN ♥KAKSDLEESKEWI⊕ RRSNOKL⊕

DSIGNWHQSSTT ♦ Transmembrane Region ♦ ♦ III ♦ LIM III LIINVT II ♦ **IAVKYY♥ R**
IQKRNRVDQN DKPYVLTNK

FIG. 25

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Fusion
Peptide
.....GLFGAI AGFIENGWEGMIDGWYGFRHQNSEGTG

▲107x178x4▲

♥ALLMOTI5♥
LVS Coiled-Coil
*Q ♥AADLKST ♠QAAIDQINGKLNRVIEKTNEKEHQIEKEFSEVEGRIQ

DLEKYVEDTKIDL* WSYNAELLVALENQHTI ♠ DLT♥ DSEMNLKFTR

RQLRENAEEMNGNGCFKIYHKCDNACIESIRNGTYDHDVYRDEALNNRFQIKG

VELKSGYKDWILWISFAISCFLLCVVLLGFIMWACQRGNIRCNICI

FIG. 26

YTSVITIELSNIKCNGTIDAKYKLI IKQELDKYKNAVTELQLLMQST
 YTSVITIELSNIKCNGTIDAKYKLI IKQELDKYK
 TSVITIELSNIKCNGTIDAKYKLI IKQELDKYK
 SVITIELSNIKCNGTIDAKYKLI IKQELDKYKNA
 VITIELSNIKCNGTIDAKYKLI IKQELDKYKNAV
 ITIELSNIKCNGTIDAKYKLI IKQELDKYKNAV
 TIELSNIKENKONGTIDAKYKLI IKQELDKYKNAVTE
 IELSNIKENKONGTIDAKYKLI IKQELDKYKNAVTEL
 ELSNIKENKONGTIDAKYKLI IKQELDKYKNAVTELQ
 LSNIKENKONGTIDAKYKLI IKQELDKYKNAVTELQ
 SNIKENKONGTIDAKYKLI IKQELDKYKNAVTELQLL
 NIKENKONGTIDAKYKLI IKQELDKYKNAVTELQLLM
 IKENKONGTIDAKYKLI IKQELDKYKNAVTELQLMQ
 KENKONGTIDAKYKLI IKQELDKYKNAVTELQLLMQS
 ENKONGTIDAKYKLI IKQELDKYKNAVTELQLLMQST

AV	CD	RSV F2	T-142	T-143	T-144	T-145	T-146	T-147	T-148	T-149	T-150	T-151	T-152	T-153	T-154	T-155
+	+/+		+	+/+	+/+	+/	+	-	-	+	-	+/	+/	+/	+/	+/
++	++		++	++	++	++	++	++	++	++	++	++	++	++	++	++

FIG. 27

AV	CD	RSV	T-67	DEFDAS SQVNEK NQSLAF IRKSDELL GEP INFYDPLVFPSDEFDAS SQVNEK NQSLAF IRKSDELLHNWNAGKSTT
++	++		T-104	INFYDPLVFPSDEFDAS SQVNEK NQSLAF IRK INFYDPLVFPSDEFDAS SQVNEK NQSLAF IRK
+-	+-		T-105	INFYDPLVFPSDEFDAS SQVNEK NQSLAF IRK INFYDPLVFPSDEFDAS SQVNEK NQSLAF IRK
+-	+-		T-106	INFYDPLVFPSDEFDAS SQVNEK NQSLAF IRK INFYDPLVFPSDEFDAS SQVNEK NQSLAF IRK
+	+		T-107	FYDPLVFPSDEFDAS SQVNEK NQSLAF IRK FYDPLVFPSDEFDAS SQVNEK NQSLAF IRK
++	++		T-108	YDPLVFPSDEFDAS SQVNEK NQSLAF IRK YDPLVFPSDEFDAS SQVNEK NQSLAF IRK
++	++		T-109	DPLVFPSDEFDAS SQVNEK NQSLAF IRK DPLVFPSDEFDAS SQVNEK NQSLAF IRK
++	++		T-110	PLVFPSDEFDAS SQVNEK NQSLAF IRK PLVFPSDEFDAS SQVNEK NQSLAF IRK
++	++		T-111	LVFPSDEFDAS SQVNEK NQSLAF IRK LVFPSDEFDAS SQVNEK NQSLAF IRK
++	++		T-112	VFPSDEFDAS SQVNEK NQSLAF IRK VFPSDEFDAS SQVNEK NQSLAF IRK
++	++		T-113	FPSDEFDAS SQVNEK NQSLAF IRK FPSDEFDAS SQVNEK NQSLAF IRK
++	++		T-114	PSDEFDAS SQVNEK NQSLAF IRK PSDEFDAS SQVNEK NQSLAF IRK
++	++		T-115	SDEFDAS SQVNEK NQSLAF IRK SDEFDAS SQVNEK NQSLAF IRK
++	++		T-116	DEFDAS SQVNEK NQSLAF IRK DEFDAS SQVNEK NQSLAF IRK
++	++		T-67	LIKE
++	++		T-117	
++	++		T-118	
++	++		T-119	

FIG. 28

AV	CD	HPF 3 178	YTPNDITLNNSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
-	-	89	YTPNDITLNNSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
-	-	90	TPNDITLNNSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
-	-	91	PNDITLNNSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
-	-	92	NDITLNNSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
-	+/-	93	DITLNNSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+/-	+/-	94	ITLNNSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+/-	+/+	95	TLNNVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+	+/+	96	LNNSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	+/+	97	NNVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	+/+	98	NSVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
-	++	99	SVALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	++	200	VALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	++	201	ALDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	++	202	LDPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	++	203	DPIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	++	204	PIDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	++	205	IDISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+++	++	206	DISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+	+	207	ISIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+	+	208	SIELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+	+	209	IELNKAKSDEESKEWIRRSNQKLDSIGNWHSQSTT
+	+	210	ELNKAKSDLEESKEWIRRSNQKLDSIGNWHSQSTT

FIG. 29

CD HPF3 107 GTIALGVATSAQITAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKEIVP
 +/+ 157 ALGVATSAQITAVALVEAKQARSDIEKLKEAIRD
 +/+ 158 LGVATSAQITAVALVEAKQARSDIEKLKEAIRDT
 +/- 159 GVATSAQITAVALVEAKQARSDIEKLKEAIRDTN
 +/+ 160 VATSAQITAVALVEAKQARSDIEKLKEAIRDTNK
 +/+ 161 ATSAQITAVALVEAKQARSDIEKLKEAIRDTNKA
 +/- 162 TSAQITAVALVEAKQARSDIEKLKEAIRDTNKAV
 +/+ 163 SAQITAVALVEAKQARSDIEKLKEAIRDTNKAVQ
 +/++ 164 AQITAVALVEAKQARSDIEKLKEAIRDTNKAVQS
 +/+ 165 QITAVALVEAKQARSDIEKLKEAIRDTNKAVQSV
 +/- 166 TAAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQ
 +/- 167 TAAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQS
 +/- 168 AAVALVEAKQARSDIEKLKEAIRDTNKAVQSVQSS
 +/- 169 AVALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSI
 +/- 170 VALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGN
 +/- 171 ALVEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGN
 +/- 172 LVEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGNL
 +/- 173 VEAKQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIV
 +/++ 174 EAKQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIV
 T-40 AKQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIV
 +/++ 175 KQARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAI
 +/++ 176 QARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIK
 +/- 177 ARSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKS
 +/- 178 RSDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSV
 - 179 SDIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQ
 - 180 DIEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQD
 - 181 IEKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDY
 - 182 EKLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYV
 +/- 183 KLKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVN
 +/++ 184 LKEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVN
 - 185 KEAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVN
 - 186 EAIRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKEIV
 - 187 AIRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKEIV
 - 188 IRDTNKAVQSVQSSIGNLIVAIKSVQDYVNKEIVP

FIG.30

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INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/05739

A. CLASSIFICATION OF SUBJECT MATTER

IPC(5) : A61K 37/02, 39/12; C12Q 1/70; G01N 33/53

US CL : 424/88, 89; 435/5, 7.1, 7.92-7.95, 974; 530/324-331, 333, 334

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 424/88, 89; 435/5, 7.1, 7.92-7.95, 974; 530/324-331, 333, 334

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, Biosis

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
NONE	NONE	NONE

 Further documents are listed in the continuation of Box C. See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
A document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
E earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
O document referring to an oral disclosure, use, exhibition or other means		
P document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

07 SEPTEMBER 1994

Date of mailing of the international search report

26 SEP 1994

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INTERNATIONAL SEARCH REPORTInternational application No.
PCT/US94/05739**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.: 2
because they relate to subject matter not required to be searched by this Authority, namely:
that the claimed subject matter is directed to mental processes.
2. Claims Nos.: 13-16 and 42-49
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
because the sequences have not been submitted to the International Searching Authority in electronic form.
3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

The additional search fees were accompanied by the applicant's protest.
 No protest accompanied the payment of additional search fees.